# **PCT**

# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau





## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6: C12N 15/12, C07K 14/47, 16/18, C12Q 1/68		(11) International Publication Number:	WO 99/31236	
		(43) International Publication Date: 24 June 1999 (24.06.		
(21) International Application Number: PCT/II	(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE			
(22) International Filing Date: 17 December 1998	(17.12.9		IS, JP, KE, KG, KP, KR, LV, MD, MG, MK, MN,	

US

US

US

(71) Applicant (for all designated States except US): GENSET [FR/FR]; 24, rue Royale, F-75008 Paris (FR).

17 December 1997 (17.12.97)

9 February 1998 (09.02.98)

10 August 1998 (10.08.98)

13 April 1998 (13.04.98)

(72) Inventors; and

(30) Priority Data:

60/069,957

60/074,121

60/081.563

60/096,116

- (75) Inventors/Applicants (for US only): BOUGUELERET, Lydie [FR/FR]; 108, avenue Victor Hugo, F-92170 Vanves (FR). DUCLERT, Aymeric [FR/FR]; 6 ter, rue Victorine, F-94100 Saint-Maur (FR). DUMAS MILNE EDWARDS, Jean-Baptiste [FR/FR]; 8, rue Grégoire de Tours, F-75006 Paris (FR).
- (74) Agents: MARTIN, Jean-Jacques et al.; Cabinet Regimbeau, 26, avenue Kléber, F-75116 Paris (FR).

B1) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

#### **Published**

Without international search report and to be republished upon receipt of that report.

(54) Title: EXTENDED cDNAs FOR SECRETED PROTEINS

## (57) Abstract

The sequences of extended cDNAs encoding secreted proteins are disclosed. The extended cDNAs can be used to express secreted proteins or portions thereof or to obtain antibodies capable of specifically binding to the secreted proteins. The extended cDNAs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. The extended cDNAs may also be used to design expression vectors and secretion vectors.

₽: `

# FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	ТJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belans	IS	Iceland	MW	Malawi	US	United States of America
	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CA CF	Central African Republic	JР	Japan	NE	Niger	VN	Viet Nam
	-	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CG	Congo Switzerland	KG	Kyrgyzstan	NO	Norway	2W	Zimbabwe
CH	•	KP	Democratic People's	NZ	New Zealand		
CI	Côte d'Ivoire	K.F	Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China		•	RO	Romania		
CU	Cuba	KZ	Kazakstan	RU	Russian Federation		
CZ	Czech Republic	rc	Saint Lucia	SD	Sudan		
DE	Germany	u	Liechtenstein				
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

WO 99/31236 PCT/IB98/02122

## EXTENDED cDNAS for secreted proteins

The present application relates to extended cDNAs which were disclosed in several United States Provisional Patent Applications. Table I lists the SEQ ID Nos. of the extended cDNAs in the present application, the SEQ ID Nos. of the identical or nearly identical extended cDNAs in the provisional applications, and the identities of the provisional applications in which the extended cDNAs were disclosed.

#### Background of the Invention

The estimated 50,000-100,000 genes scattered along the human chromosomes offer tremendous promise for the understanding, diagnosis, and treatment of human diseases. In addition, probes capable of specifically hybridizing to loci distributed throughout the human genome find applications in the construction of high resolution chromosome maps and in the identification of individuals.

In the past, the characterization of even a single human gene was a painstaking process, requiring years of effort. Recent developments in the areas of cloning vectors, DNA sequencing, and computer technology have merged to greatly accelerate the rate at which human genes can be isolated, sequenced, mapped, and characterized. Cloning vectors such as yeast artificial chromosomes (YACs) and bacterial artificial chromosomes (BACs) are able to accept DNA inserts ranging from 300 to 1000 kilobases (kb) or 100-400 kb in length respectively, thereby facilitating the manipulation and ordering of DNA sequences distributed over great distances on the human chromosomes. Automated DNA sequencing machines permit the rapid sequencing of human genes. Bioinformatics software enables the comparison of nucleic acid and protein sequences, thereby assisting in the characterization of human gene products.

Currently, two different approaches are being pursued for identifying and characterizing the genes distributed along the human genome. In one approach, large fragments of genomic DNA are isolated, cloned, and sequenced. Potential open reading frames in these genomic sequences are identified using bio-informatics software. However, this approach entails sequencing large stretches of human DNA which do not encode proteins in order to find the protein encoding sequences scattered throughout the genome. In addition to requiring extensive sequencing, the bio-informatics software may mischaracterize the genomic sequences obtained. Thus, the software may produce false positives in which non-coding DNA is mischaracterized as coding DNA or false negatives in which coding DNA is mischaracterized as non-coding DNA.

An alternative approach takes a more direct route to identifying and characterizing human genes. In this approach, complementary DNAs (cDNAs) are synthesized from isolated messenger RNAs (mRNAs) which encode human proteins. Using this approach, sequencing is only performed on DNA which is derived from protein coding portions of the genome. Often, only short stretches of the cDNAs are sequenced to obtain sequences called expressed sequence tags (ESTs). The ESTs may then be used to isolate or purify extended cDNAs which include sequences adjacent to the EST sequences. The extended cDNAs may contain all of the sequence of the EST which was used to obtain them or only a portion of the sequence of the EST which was used to obtain them. In addition, the extended cDNAs may contain the full coding sequence of the gene from which the EST was derived or, alternatively, the extended cDNAs may include

portions of the coding sequence of the gene from which the EST was derived. It will be appreciated that there may be several extended cDNAs which include the EST sequence as a result of alternate splicing or the activity of alternative promoters.

In the past, the short EST sequences which could be used to isolate or purify extended cDNAs were often 5 obtained from oligo-dT primed cDNA libraries. Accordingly, they mainly corresponded to the 3' untranslated region of the mRNA. In part, the prevalence of EST sequences derived from the 3' end of the mRNA is a result of the fact that typical techniques for obtaining cDNAs, are not well suited for isolating cDNA sequences derived from the 5' ends of mRNAs. (Adams et al., Nature 377:174, 1996, Hillier et al., Genome Res. 6:807-828, 1996).

In addition, in those reported instances where longer cDNA sequences have been obtained, the reported 10 sequences typically correspond to coding sequences and do not include the full 5' untranslated region of the mRNA from which the cDNA is derived. Such incomplete sequences may not include the first exon of the mRNA, particularly in situations where the first exon is short. Furthermore, they may not include some exons, often short ones, which are located upstream of splicing sites. Thus, there is a need to obtain sequences derived from the 5' ends of mRNAs which can be used to obtain extended cDNAs which may include the 5' sequences contained in the 5' ESTs.

While many sequences derived from human chromosomes have practical applications, approaches based on the identification and characterization of those chromosomal sequences which encode a protein product are particularly relevant to diagnostic and therapeutic uses. Of the 50,000-100,000 protein coding genes, those genes encoding proteins which are secreted from the cell in which they are synthesized, as well as the secreted proteins themselves, are particularly valuable as potential therapeutic agents. Such proteins are often involved in cell to cell communication and 20 may be responsible for producing a clinically relevant response in their target cells.

In fact, several secretory proteins, including tissue plasminogen activator, G-CSF, GM-CSF, erythropoietin, human growth hormone, insulin, interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , and interleukin-2, are currently in clinical use. These proteins are used to treat a wide range of conditions, including acute myocardial infarction, acute ischemic stroke, anemia, diabetes, growth hormone deficiency, hepatitis, kidney carcinoma, chemotherapy induced neutropenia and 25 multiple sclerosis. For these reasons, extended cDNAs encoding secreted proteins or portions thereof represent a particularly valuable source of therapeutic agents. Thus, there is a need for the identification and characterization of secreted proteins and the nucleic acids encoding them.

In addition to being therapeutically useful themselves, secretory proteins include short peptides, called signal peptides, at their amino termini which direct their secretion. These signal peptides are encoded by the signal sequences 30 located at the 5' ends of the coding sequences of genes encoding secreted proteins. Because these signal peptides will direct the extracellular secretion of any protein to which they are operably linked, the signal sequences may be exploited to direct the efficient secretion of any protein by operably linking the signal sequences to a gene encoding the protein for which secretion is desired. This may prove beneficial in gene therapy strategies in which it is desired to deliver a particular gene product to cells other than the cell in which it is produced. Signal sequences encoding signal peptides

also find application in simplifying protein purification techniques. In such applications, the extracellular secretion of the desired protein greatly facilitates purification by reducing the number of undesired proteins from which the desired protein must be selected. Thus, there exists a need to identify and characterize the 5' portions of the genes for secretory proteins which encode signal peptides.

Public information on the number of human genes for which the promoters and upstream regulatory regions have been identified and characterized is quite limited. In part, this may be due to the difficulty of isolating such regulatory sequences. Upstream regulatory sequences such as transcription factor binding sites are typically too short to be utilized as probes for isolating promoters from human genomic libraries. Recently, some approaches have been developed to isolate human promoters. One of them consists of making a CpG island library (Cross, S.H. et al., 10 Purification of CpG Islands using a Methylated DNA Binding Column, Nature Genetics 6: 236-244 (1994)). The second consists of isolating human genomic DNA sequences containing Spel binding sites by the use of Spel binding protein. (Mortlock et al., Genome Res. 6:327-335, 1996). Both of these approaches have their limits due to a lack of specificity or of comprehensiveness.

5' ESTs and extended cDNAs obtainable therefrom may be used to efficiently identify and isolate upstream 15 regulatory regions which control the location, developmental stage, rate, and quantity of protein synthesis, as well as the stability of the mRNA. (Theil et al., BioFactors 4:87-93, (1993). Once identified and characterized, these regulatory regions may be utilized in gene therapy or protein purification schemes to obtain the desired amount and locations of protein synthesis or to inhibit, reduce, or prevent the synthesis of undesirable gene products.

In addition, ESTs containing the 5' ends of secretory protein genes or extended cDNAs which include 20 sequences adjacent to the sequences of the ESTs may include sequences useful as probes for chromosome mapping and the identification of individuals. Thus, there is a need to identify and characterize the sequences upstream of the 5' coding sequences of genes encoding secretory proteins.

#### Summary of the Invention

The present invention relates to purified, isolated, or recombinant extended cDNAs which encode secreted 25 proteins or fragments thereof. Preferably, the purified, isolated or recombinant cDNAs contain the entire open reading frame of their corresponding mRNAs, including a start codon and a stop codon. For example, the extended cDNAs may include nucleic acids encoding the signal peptide as well as the mature protein. Alternatively, the extended cDNAs may contain a fragment of the open reading frame. In some embodiments, the fragment may encode only the sequence of the mature protein. Alternatively, the fragment may encode only a portion of the mature protein. A further aspect of the present invention is a nucleic acid which encodes the signal peptide of a secreted protein.

The present extended cDNAs were obtained using ESTs which include sequences derived from the authentic 5' ends of their corresponding mRNAs. As used herein the terms "EST" or "5' EST" refer to the short cDNAs which were used to obtain the extended cDNAs of the present invention. As used herein, the term "extended cDNA" refers to the cDNAs which include sequences adjacent to the 5' EST used to obtain them. The extended cDNAs may contain all or a

portion of the sequence of the EST which was used to obtain them. The term "corresponding mRNA" refers to the mRNA which was the template for the cDNA synthesis which produced the 5' EST. As used herein, the term "purified" does not require absolute purity; rather, it is intended as a relative definition. Individual extended cDNA clones isolated from a cDNA library have been conventionally purified to electrophoretic homogeneity. The sequences obtained from these clones could not be obtained directly either from the library or from total human DNA. The extended cDNA clones are not naturally occurring as such, but rather are obtained via manipulation of a partially purified naturally occurring substance (messenger RNA). The conversion of mRNA into a cDNA library involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection. Thus, creating a cDNA library from messenger RNA and subsequently isolating individual clones from that library results in an approximately 104-106 fold purification of the native message. Purification of starting material or natural material to at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated.

As used herein, the term "isolated" requires that the material be removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide present in a living animal is not isolated, but the same polynucleotide, separated from some or all of the coexisting materials in the natural system, is isolated.

As used herein, the term "recombinant" means that the extended cDNA is adjacent to "backbone" nucleic acid to which it is not adjacent in its natural environment. Additionally, to be "enriched" the extended cDNAs will represent 5% or more of the number of nucleic acid inserts in a population of nucleic acid backbone molecules. Backbone molecules according to the present invention include nucleic acids such as expression vectors, self-replicating nucleic acids, viruses, integrating nucleic acids, and other vectors or nucleic acids used to maintain or manipulate a nucleic acid insert of interest. Preferably, the enriched extended cDNAs represent 15% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. More preferably, the enriched extended cDNAs represent 50% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. In a highly preferred embodiment, the enriched extended cDNAs represent 90% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. "Stringent", "moderate," and "low" hybridization conditions are as defined in Example 29.

Unless otherwise indicated, a "complementary" sequence is fully complementary. Thus, extended cDNAs encoding secreted polypeptides or fragments thereof which are present in cDNA libraries in which one or more extended cDNAs encoding secreted polypeptides or fragments thereof make up 5% or more of the number of nucleic acid inserts in the backbone molecules are "enriched recombinant extended cDNAs" as defined herein. Likewise, extended cDNAs encoding secreted polypeptides or fragments thereof which are in a population of plasmids in which one or more extended cDNAs of the present invention have been inserted such that they represent 5% or more of the number of inserts in the plasmid backbone are "enriched recombinant extended cDNAs" as defined herein. However, extended

cDNAs encoding secreted polypeptides or fragments thereof which are in cDNA libraries in which the extended cDNAs encoding secreted polypeptides or fragments thereof constitute less than 5% of the number of nucleic acid inserts in the population of backbone molecules, such as libraries in which backbone molecules having a cDNA insert encoding a secreted polypeptide are extremely rare, are not "enriched recombinant extended cDNAs."

In particular, the present invention relates to extended cDNAs which were derived from genes encoding secreted proteins. As used herein, a "secreted" protein is one which, when expressed in a suitable host cell, is transported across or through a membrane, including transport as a result of signal peptides in its amino acid sequence. "Secreted" proteins include without limitation proteins secreted wholly (e.g. soluble proteins), or partially (e.g. receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins which are 10 transported across the membrane of the endoplasmic reticulum.

Extended cDNAs encoding secreted proteins may include nucleic acid sequences, called signal sequences, which encode signal puptides which direct the extracellular secretion of the proteins encoded by the extended cDNAs. Generally, the signal peptides are located at the amino termini of secreted proteins.

Secreted proteins are translated by ribosomes associated with the "rough" endoplasmic reticulum. Generally, 15 secreted proteins are co-translationally transferred to the membrane of the endoplasmic reticulum. Association of the ribosome with the endoplasmic reticulum during translation of secreted proteins is mediated by the signal peptide. The signal peptide is typically cleaved following its co-translational entry into the endoplasmic reticulum. After delivery to the endoplasmic reticulum, secreted proteins may proceed through the Golgi apparatus. In the Golgi apparatus, the proteins may undergo post-translational modification before entering secretory vesicles which transport them across the 20 cell membrane.

The extended cDNAs of the present invention have several important applications. For example, they may be used to express the entire secreted protein which they encode. Alternatively, they may be used to express portions of the secreted protein. The portions may comprise the signal peptides encoded by the extended cDNAs or the mature proteins encoded by the extended cDNAs (i.e. the proteins generated when the signal peptide is cleaved off). The 25 portions may also comprise polypeptides having at least 10 consecutive amino acids encoded by the extended cDNAs. Alternatively, the portions may comprise at least 15 consecutive amino acids encoded by the extended cDNAs. In some embodiments, the portions may comprise at least 25 consecutive amino acids encoded by the extended cDNAs. In other embodiments, the portions may comprise at least 40 amino acids encoded by the extended cDNAs.

Antibodies which specifically recognize the entire secreted proteins encoded by the extended cDNAs or 30 fragments thereof having at least 10 consecutive amino acids, at least 15 consecutive amino acids, at least 25 consecutive amino acids, or at least 40 consecutive amino acids may also be obtained as described below. Antibodies which specifically recognize the mature protein generated when the signal peptide is cleaved may also be obtained as described below. Similarly, antibodies which specifically recognize the signal peptides encoded by the extended cDNAs may also be obtained.

In some embodiments, the extended cDNAs include the signal sequence. In other embodiments, the extended cDNAs may include the full coding sequence for the mature protein (i.e. the protein generated when the signal polypeptide is cleaved off). In addition, the extended cDNAs may include regulatory regions upstream of the translation start site or downstream of the stop codon which control the amount, location, or developmental stage of gene expression. As discussed above, secreted proteins are therapeutically important. Thus, the proteins expressed from the cDNAs may be useful in treating or controlling a variety of human conditions. The extended cDNAs may also be used to obtain the corresponding genomic DNA. The term "corresponding genomic DNA" refers to the genomic DNA which encodes mRNA which includes the sequence of one of the strands of the extended cDNA in which thymidine residues in the sequence of the extended cDNA are replaced by uracil residues in the mRNA.

The extended cDNAs or genomic DNAs obtained therefrom may be used in forensic procedures to identify individuals or in diagnostic procedures to identify individuals having genetic diseases resulting from abnormal expression of the genes corresponding to the extended cDNAs. In addition, the present invention is useful for constructing a high resolution map of the human chromosomes.

The present invention also relates to secretion vectors capable of directing the secretion of a protein of

interest. Such vectors may be used in gene therapy strategies in which it is desired to produce a gene product in one cell which is to be delivered to another location in the body. Secretion vectors may also facilitate the purification of desired proteins.

The present invention also relates to expression vectors capable of directing the expression of an inserted gene in a desired spatial or temporal manner or at a desired level. Such vectors may include sequences upstream of the extended cDNAs such as promoters or upstream regulatory sequences.

In addition, the present invention may also be used for gene therapy to control or treat genetic diseases. Signal peptides may also be fused to heterologous proteins to direct their extracellular secretion.

One embodiment of the present invention is a purified or isolated nucleic acid comprising the sequence of one of SEO ID NOs: 40-140 and 242-377 or a sequence complementary thereto. In one aspect of this embodiment, the nucleic acid is recombinant.

Another embodiment of the present invention is a purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 40-140 and 242-377 or one of the sequences complementary thereto. In one aspect of this embodiment, the nucleic acid comprises at least 15, 25, 30, 40, 50, 75, or 100 consecutive bases of one of the sequences of SEQ ID NOs: 40-140 and 242-377 or one of the sequences complementary thereto. The nucleic acid may be a recombinant nucleic acid.

Another embodiment of the present invention is a purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent conditions to the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary to one of the sequences of SEQ ID NOs: 40-140 and 242-377. In one aspect of this embodiment, the nucleic acid is recombinant.

30

۱۲,

Another embodiment of the present invention is a purified or isolated nucleic acid comprising the full coding sequences of one of SEQ ID NOs: 40-140 and 242-377, wherein the full coding sequence optionally comprises the sequence encoding signal peptide as well as the sequence encoding mature protein. In a preferred embodiment, the isolated or purified nucleic acid comprises the full coding sequence of one of SEQ ID Nos. 40, 42-44, 46, 48, 49, 51, 53, 60, 62-72, 76-78, 80-83, 85-88, 90, 93, 94, 97, 99-102, 104, 107-125, 127, 132, 135-138, 140 and 242-377 wherein the full coding sequence comprises the sequence encoding signal peptide and the sequence encoding mature protein. In one aspect of this embodiment, the nucleic acid is recombinant.

A further embodiment of the present invention is a purified or isolated nucleic acid comprising the nucleotides of one of SEO ID NOs: 40-140 and 242-377 which encode a mature protein. In a preferred embodiment, the purified or isolated nucleic acid comprises the nucleotides of one of SEO ID NOs: 40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode a mature protein. In one aspect of this embodiment, the nucleic acid is recombinant.

Yet another embodiment of the present invention is a purified or isolated nucleic acid comprising the nucleotides of one of SEO ID NOs: 40-140 and 242-377 which encode the signal peptide. In a preferred embodiment, the purified or isolated nucleic acid comprises the nucleotides of SEO ID NOs: 40, 42-46, 48, 49, 51, 53, 57, 60, 62-73, 76-78, 80-83, 85-88, 90, 93-95, 97, 99-102, 104, 107-125, 127, 128, 130, 132, 134-140 and 242-377 which encode the signal peptide. In one aspect of this embodiment, the nucleic acid is recombinant.

Another embodiment of the present invention is a purified or isolated nucleic acid encoding a polypeptide having the sequence of one of the sequences of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is a purified or isolated nucleic acid encoding a polypeptide having the sequence of a mature protein included in one of the sequences of SEO ID NOs: 141-241 and 378-513. In a preferred embodiment, the purified or isolated nucleic acid encodes a polypeptide having the sequence of a mature protein included in one of the sequences of SEO ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.

Another embodiment of the present invention is a purified or isolated nucleic acid encoding a polypeptide having the sequence of a signal peptide included in one of the sequences of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the purified or isolated nucleic acid encodes a polypeptide having the sequence of a signal peptide included in one of the sequences of SEQ ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.

Yet another embodiment of the present invention is a purified or isolated protein comprising the sequence of one of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is a purified or isolated polypeptide comprising at least 10 consecutive amino acids of one of the sequences of SEO ID NOs: 141-241 and 378-513. In one aspect of this embodiment, the purified or isolated polypeptide comprises at least 15, 20, 25, 35, 50, 75, 100, 150 or 200 consecutive

amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In still another aspect, the purified or isolated polypeptide comprises at least 25 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is an isolated or purified polypeptide comprising a signal peptide of one of the polypeptides of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the isolated or purified polypeptide comprises a signal peptide of one of the polypeptides of SEQ ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.

Yet another embodiment of the present invention is an isolated or purified polypeptide comprising a mature protein of one of the polypeptides of SEQ ID NOs: 141-241 and 378-513. In a preferred embodiment, the isolated or purified polypeptide comprises a mature protein of one of the polypeptides of SEQ ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.

A further embodiment of the present invention is a method of making a protein comprising one of the sequences of SEQ ID NO: 141-241 and 378-513, comprising the steps of obtaining a cDNA comprising one of the sequences of sequence of SEQ ID NO: 40-140 and 242-377, inserting the cDNA in an expression vector such that the cDNA is operably linked to a promoter, and introducing the expression vector into a host cell whereby the host cell produces the protein encoded by said cDNA. In one aspect of this embodiment, the method further comprises the step of isolating the protein.

Another embodiment of the present invention is a protein obtainable by the method described in the preceding paragraph.

Another embodiment of the present invention is a method of making a protein comprising the amino acid sequence of the mature protein contained in one of the sequences of SEQ ID NO: 141-241 and 378-513, comprising the steps of obtaining a cDNA comprising one of the nucleotides sequence of sequence of SEQ ID NO: 40-140 and 242-377 which encode for the mature protein, inserting the cDNA in an expression vector such that the cDNA is operably linked to a promoter, and introducing the expression vector into a host cell whereby the host cell produces the mature protein encoded by the cDNA. In one aspect of this embodiment, the method further comprises the step of isolating the protein.

Another embodiment of the present invention is a mature protein obtainable by the method described in the preceding paragraph.

In a preferred embodiment, the above method comprises a method of making a protein comprising the amino acid sequence of the mature protein contained in one of the sequences of SEO ID NO: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513, comprising the steps of obtaining a cDNA comprising one of the nucleotides sequence of sequence of SEO ID NO:

4,10

40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode for the mature protein, inserting the cDNA in an expression vector such that the cDNA is operably linked to a promoter, and introducing the expression vector into a host cell whereby the host cell produces the mature protein encoded by the cDNA. In one aspect of this embodiment, the method further comprises the step of 5 isolating the protein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the sequence of one of SEQ ID NOs: 40-140 and 242-377 or a sequence complementary thereto described herein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids

comprising the full coding sequences of one of SEO ID NOs: 40-140 and 242-377, wherein the full coding sequence

comprises the sequence encoding signal peptide and the sequence encoding mature protein described herein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the nucleotides of one of SEO ID NOs: 40-140 and 242-377 which encode a mature protein which are described herein. Preferably, the host cell contains the purified or isolated nucleic acids comprising the nucleotides of one of SEO ID NOs: 40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode a mature protein.

Another embodiment of the present invention is a host cell containing the purified or isolated nucleic acids comprising the nucleotides of one of SEQ ID NOs: 40-140 and 242-377 which encode the signal peptide which are described herein. Preferably, the host cell contains the purified or isolated nucleic acids comprising the nucleotides of one of SEQ ID Nos.: 40, 42-46, 48, 49, 51, 53, 57, 60, 62-73, 76-78, 80-83, 85-88, 90, 93-95, 97, 99-102, 104, 107-125, 127, 128, 130, 132, 134-140 and 242-377 which encode the signal peptide.

Another embodiment of the present invention is a purified or isolated antibody capable of specifically binding to a protein having the sequence of one of SEQ ID NOs: 141-241 and 378-513. In one aspect of this embodiment, the antibody is capable of binding to a polypeptide comprising at least 10 consecutive amino acids of the sequence of one of SEQ ID NOs: 141-241 and 378-513.

Another embodiment of the present invention is an array of cDNAs or fragments thereof of at least 15 nucleotides in length which includes at least one of the sequences of SEO ID NOs: 40-140 and 242-377, or one of the sequences complementary to the sequences of SEO ID NOs: 40-140 and 242-377, or a fragment thereof of at least 15 consecutive nucleotides. In one aspect of this embodiment, the array includes at least two of the sequences of SEO ID NOs: 40-140 and 242-377, or fragments thereof of at least 15 consecutive nucleotides. In another aspect of this embodiment, the array includes at least five of the sequences of SEO ID NOs: 40-140 and 242-377, the sequences complementary to the sequences of SEO ID NOs: 40-140 and 242-377, or fragments thereof of at least 15 consecutive nucleotides.

A further embodiment of the invention encompasses purified polynucleotides comprising an insert from a clone deposited in a deposit having an accession number selected from the group consisting of the accession numbers listed in Table VI or a fragment thereof comprising a contiguous span of at least 8, 10, 12, 15, 20, 25, 40, 60, 100, or 200 nucleotides of said insert. An additional embodiment of the invention encompasses purified polypeptides which comprise, consist of, or consist essentially of an amino acid sequence encoded by the insert from a clone deposited in a deposit having an accession number selected from the group consisting of the accession numbers listed in Table VI, as well as polypeptides which comprise a fragment of said amino acid sequence consisting of a signal peptide, a mature protein, or a contiguous span of at least 5, 8, 10, 12, 15, 20, 25, 40, 60, 100, or 200 amino acids encoded by said insert.

An additional embodiment of the invention encompasses purified polypeptides which comprise a contiguous span of at least 5, 8, 10, 12, 15, 20, 25, 40, 60, 100, or 200 amino acids of SEO ID NOs: 158, 174, 175, 196, 226, 231, 232, wherein said contiguous span comprises at least one of the amino acid positions which was not shown to be identical to a public sequence in any of Figures 11 to 15. Also encompassed by the invention are purified polypuculeotides encoding said polypeptides.

15

10

## **Brief Description of the Drawings**

Figure 1 is a summary of a procedure for obtaining cDNAs which have been selected to include the 5' ends of the mRNAs from which they are derived.

Figure 2 is an analysis of the 43 amino terminal amino acids of all human SwissProt proteins to determine the 20 frequency of false positives and false negatives using the techniques for signal peptide identification described herein.

Figure 3 shows the distribution of von Heijne scores for 5' ESTs in each of the categories described herein and the probability that these 5' ESTs encode a signal peptide.

Figure 4 shows the distribution of 5' ESTs in each category and the number of 5' ESTs in each category having a given minimum von Heijne's score.

Figure 5 shows the tissues from which the mRNAs corresponding to the 5' ESTs in each of the categories described herein were obtained.

Figure 6 illustrates a method for obtaining extended cDNAs.

Figure 7 is a map of pED6dpc2. pED6dpc2 is derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning. SSt cDNAs are cloned between EcoRI and Notl. PED vectors are described in Kaufman et al. 30 (1991), NAR 19: 4485-4490.

Figure 8 provides a schematic description of the promoters isolated and the way they are assembled with the corresponding 5' tags.

Figure 9 describes the transcription factor binding sites present in each of these promoters.

Figure 10 is an alignment of the protein of SEO ID NO: 217 with the human protein TFAR19 that may play a role in apoptosis (Genbank accession number AF014955, SEO ID NO: 516).

Figure 11 is an alignment of the proteins of SEQ ID NOs: 174, 175 and 232 with a human secreted protein (Genseq accession number W36955, SEQ ID NO: 517).

Figure 12 is an alignment of the protein of SEQ ID NO: 231 with the human E25 protein (Genbank accession number AF038953, SEQ ID NO: 515).

Figure 13 is an alignment of the protein of SEQ ID NO: 196 with the human seventransmembrane protein (Genbank accession number Y11395, SEQ ID NO: 518).

Figure 14 is an alignment of the protein of SEQ ID NOs: 158 with the murine subunit 7a of the COP9 complex 10 (Genbank accession number AF071316, SEQ ID NO: 519).

Figure 15 is an alignment of the protein of SEQ ID NO: 226 with the bovine subunit B14.5B of the NADHubiquinone oxidureductase complex (Arizmendi *et al, FEBS Lett.*, **313**: 80-84 (1992) and Swissprot accession -number Q02827, SEQ ID NO: 514).

## **Detailed Description of the Preferred Embodiment**

## 15 I. Obtaining 5' ESTs

The present extended cDNAs were obtained using 5' ESTs which were isolated as described below.

## A. Chemical Methods for Obtaining mRNAs having Intact 5' Ends

In order to obtain the 5' ESTs used to obtain the extended cDNAs of the present invention, mRNAs having intact 5' ends must be obtained. Currently, there are two approaches for obtaining such mRNAs. One of these 20 approaches is a chemical modification method involving derivatization of the 5' ends of the mRNAs and selection of the derivatized mRNAs. The 5' ends of eucaryotic mRNAs possess a structure referred to as a "cap" which comprises a guanosine methylated at the 7 position. The cap is joined to the first transcribed base of the mRNA by a 5', 5'. triphosphate bond. In some instances, the 5' guanosine is methylated in both the 2 and 7 positions. Rarely, the 5'guanosine is trimethylated at the 2, 7 and 7 positions. In the chemical method for obtaining mRNAs having intact 5' 25 ends, the 5' cap is specifically derivatized and coupled to a reactive group on an immobilizing substrate. This specific derivatization is based on the fact that only the ribose linked to the methylated guanosine at the 5' end of the mRNA and the ribose linked to the base at the 3' terminus of the mRNA, possess 2', 3'-cis diols. Optionally, where the 3' terminal ribose has a 2', 3'-cis diol, the 2', 3'-cis diol at the 3' end may be chemically modified, substituted, converted, or eliminated, leaving only the ribose linked to the methylated guanosine at the 5' end of the mRNA with a 2', 3'-cis diol. A 30 variety of techniques are available for eliminating the 2', 3'-cis diol on the 3' terminal ribose. For example, controlled alkaline hydrolysis may be used to generate mRNA fragments in which the 3' terminal ribose is a 3'-phosphate, 2'phosphate or (2', 3')-cyclophosphate. Thereafter, the fragment which includes the original 3' ribose may be eliminated from the mixture through chromatography on an oligo-dT column. Alternatively, a base which lacks the 2', 3'-cis diol

may be added to the 3' end of the mRNA using an RNA ligase such as T4 RNA ligase. Example 1 below describes a method for ligation of pCp to the 3' end of messenger RNA.

## **EXAMPLE 1**

## Ligation of the Nucleoside Diphosphate pCp to the 3' End of Messenger RNA

5 1 μg of RNA was incubated in a final reaction medium of 10 μl in the presence of 5 U of T<sub>4</sub> phage RNA ligase in the buffer provided by the manufacturer (Gibco - BRL), 40 U of the RNase inhibitor RNasin (Promega) and, 2 µl of <sup>32</sup>pCp (Amersham #PB 10208).

The incubation was performed at 37°C for 2 hours or overnight at 7-8°C.

Following modification or elimination of the 2', 3'-cis diol at the 3' ribose, the 2', 3'-cis diol present at the 5' 10 end of the mRNA may be oxidized using reagents such as NaBH, NaBH, CN, or sodium periodate, thereby converting the 2', 3'-cis diol to a dialdehyde. Example 2 describes the oxidation of the 2', 3'-cis diol at the 5' end of the mRNA with sodium periodate.

## **EXAMPLE 2**

## Oxidation of 2', 3'-cis diol at the 5' End of the mRNA

0.1 OD unit of either a capped oligoribonucleotide of 47 nucleotides (including the cap) or an uncapped oligoribonucleotide of 46 nucleotides were treated as follows. The oligoribonucleotides were produced by in vitro transcription using the transcription kit "AmpliScribe T7" (Epicentre Technologies). As indicated below, the DNA template for the RNA transcript contained a single cytosine. To synthesize the uncapped RNA, all four NTPs were included in the in vitro transcription reaction. To obtain the capped RNA, GTP was replaced by an analogue of the cap, 20 m7G(5')ppp(5')G. This compound, recognized by polymerase, was incorporated into the 5' end of the nascent transcript during the step of initiation of transcription but was not capable of incorporation during the extension step. Consequently, the resulting RNA contained a cap at its 5' end. The sequences of the oligoribonucleotides produced by the in vitro transcription reaction were:

+ Cap:

15

- 25 5'm7GpppGCAUCCUACUCCCAUCCAAUUCCACCUAACUCCCCAUCUCCAC-3' (SEO ID NO:1)

5'-pppGCAUCCUACUCCCAUCCAAUUCCACCCUAACUCCUCCCAUCUCCAC-3' (SEQ ID NO:2)

The oligoribonucleotides were dissolved in 9 µl of acetate buffer (0.1 M sodium acetate, pH 5.2) and 3 µl of freshly prepared 0.1 M sodium periodate solution. The mixture was incubated for 1 hour in the dark at 4°C or room 30 temperature. Thereafter, the reaction was stopped by adding 4 µl of 10% ethylene glycol. The product was ethanol precipitated, resuspended in 10µl or more of water or appropriate buffer and dialyzed against water.

The resulting aldehyde groups may then be coupled to molecules having a reactive amine group, such as hydrazine, carbazide, thiocarbazide or semicarbazide groups, in order to facilitate enrichment of the 5' ends of the mRNAs. Molecules having reactive amine groups which are suitable for use in selecting mRNAs having intact 5' ends include avidin, proteins, antibodies, vitamins, ligands capable of specifically binding to receptor molecules, or oligonucleotides. Example 3 below describes the coupling of the resulting dialdehyde to biotin.

### **EXAMPLE 3**

## Coupling of the Dialdehyde with Biotin

The oxidation product obtained in Example 2 was dissolved in 50 µl of sodium acetate at a pH of between 5 and 5.2 and 50 µl of freshly prepared 0.02 M solution of biotin hydrazide in a methoxyethanol/water mixture (1:1) of formula:

In the compound used in these experiments, n = 5. However, it will be appreciated that other commercially available hydrazides may also be used, such as molecules of the formula above in which n varies from 0 to 5.

The mixture was then incubated for 2 hours at 37°C. Following the incubation, the mixture was precipitated with ethanol and dialyzed against distilled water.

Example 4 demonstrates the specificity of the biotinylation reaction.

15

### **EXAMPLE 4**

## **Specificity of Biotinylation**

The specificity of the biotinylation for capped mRNAs was evaluated by gel electrophoresis of the following samples:

- Sample 1. The 46 nucleotide uncapped in vitro transcript prepared as in Example 2 and labeled with <sup>32</sup>pCp as 20 described in Example 1.
  - Sample 2. The 46 nucleotide uncapped in vitro transcript prepared as in Example 2, labeled with <sup>32</sup>pCp as described in Example 1, treated with the oxidation reaction of Example 2, and subjected to the biotinylation conditions of Example 3.
- Sample 3. The 47 nucleotide capped in vitro transcript prepared as in Example 2 and labeled with <sup>32</sup>pCp as described in Example 1.
  - Sample 4. The 47 nucleotide capped in vitro transcript prepared as in Example 2, labeled with <sup>32</sup>pCp as described in Example 1, treated with the oxidation reaction of Example 2, and subjected to the biotinylation conditions of Example 3.
- Samples 1 and 2 had indentical migration rates, demonstrating that the uncapped RNAs were not oxidized and biotinylated. Sample 3 migrated more slowly than Samples 1 and 2, while Sample 4 exhibited the slowest migration.

: :

25

The difference in migration of the RNAs in Samples 3 and 4 demonstrates that the capped RNAs were specifically biotinylated.

In some cases, mRNAs having intact 5' ends may be enriched by binding the molecule containing a reactive amine group to a suitable solid phase substrate such as the inside of the vessel containing the mRNAs, magnetic beads, 5 chromatography matrices, or nylon or nitrocellulose membranes. For example, where the molecule having a reactive amine group is biotin, the solid phase substrate may be coupled to avidin or streptavidin. Alternatively, where the molecule having the reactive amine group is an antibody or receptor ligand, the solid phase substrate may be coupled to the cognate antigen or receptor. Finally, where the molecule having a reactive amine group comprises an oligonucleotide, the solid phase substrate may comprise a complementary oligonucleotide.

The mRNAs having intact 5' ends may be released from the solid phase following the enrichment procedure. For example, where the dialdehyde is coupled to biotin hydrazide and the solid phase comprises streptavidin, the mRNAs may be released from the solid phase by simply heating to 95 degrees Celsius in 2% SDS. In some methods, the molecule having a reactive amine group may also be cleaved from the mRNAs having intact 5' ends following enrichment. Example 5 describes the capture of biotinylated mRNAs with streptavidin coated beads and the release of the 1,5 biotinylated mRNAs from the beads following enrichment.

## **EXAMPLE 5**

## Capture and Release of Biotinylated mRNAs Using Strepatividin Coated Beads

The streptavidin-coated magnetic beads were prepared according to the manufacturer's instructions (CPG Inc., USA). The biotinylated mRNAs were added to a hybridization buffer (1.5 M NaCl, pH 5 - 6). After incubating for 30 20 minutes, the unbound and nonbiotinylated material was removed. The beads were washed several times in water with 1% SDS. The beads obtained were incubated for 15 minutes at 95°C in water containing 2% SDS.

Example 6 demonstrates the efficiency with which biotinylated mRNAs were recovered from the streptavidin coated beads.

## **EXAMPLE 6**

# Efficiency of Recovery of Biotinylated mRNAs

The efficiency of the recovery procedure was evaluated as follows. RNAs were labeled with 32pCp, oxidized, biotinylated and bound to streptavidin coated beads as described above. Subsequently, the bound RNAs were incubated for 5, 15 or 30 minutes at 95°C in the presence of 2% SDS.

The products of the reaction were analyzed by electrophoresis on 12% polyacrylamide gels under denaturing 30 conditions (7 M urea). The gels were subjected to autoradiography. During this manipulation, the hydrazone bonds were not reduced.

Increasing amounts of nucleic acids were recovered as incubation times in 2% SDS increased, demonstrating that biotinylated mRNAs were efficiently recovered.

In an alternative method for obtaining mRNAs having intact 5' ends, an oligonucleotide which has been derivatized to contain a reactive amine group is specifically coupled to mRNAs having an intact cap. Preferably, the 3' end of the mRNA is blocked prior to the step in which the aldehyde groups are joined to the derivatized oligonucleotide, as described above, so as to prevent the derivatized oligonucleotide from being joined to the 3' end of the mRNA. For example, pCp may be attached to the 3' end of the mRNA using T4 RNA ligase. However, as discussed above, blocking the 3' end of the mRNA is an optional step. Derivatized oligonucleotides may be prepared as described below in Example 7.

### **EXAMPLE 7**

## Derivatization of the Oligonucleotide

An oligonucleotide phosphorylated at its 3' end was converted to a 3' hydrazide in 3' by treatment with an aqueous solution of hydrazine or of dihydrazide of the formula H<sub>2</sub>N(R1)NH<sub>2</sub> at about 1 to 3 M, and at pH 4.5, in the presence of a carbodiimide type agent soluble in water such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide at a final concentration of 0.3 M at a temperature of 8°C overnight.

The derivatized oligonucleotide was then separated from the other agents and products using a standard technique for isolating oligonucleotides.

As discussed above, the mRNAs to be enriched may be treated to eliminate the 3' OH groups which may be present thereon. This may be accomplished by enzymatic ligation of sequences lacking a 3' OH, such as pCp, as described above in Example 1. Alternatively, the 3' OH groups may be eliminated by alkaline hydrolysis as described in Example 8 below.

## 20

25

#### **EXAMPLE 8**

## Alkaline Hydrolysis of mRNA

The mRNAs may be treated with alkaline hydrolysis as follows. In a total volume of  $100\mu$ l of 0.1N sodium hydroxide, 1.5 $\mu$ g mRNA is incubated for 40 to 60 minutes at 4°C. The solution is neutralized with acetic acid and precipitated with ethanol.

Following the optional elimination of the 3' OH groups, the diol groups at the 5' ends of the mRNAs are oxidized as described below in Example 9.

#### **EXAMPLE 9**

## **Oxidation of Diols**

Up to 1 OD unit of RNA was dissolved in 9 µl of buffer (0.1 M sodium acetate, pH 6-7 or water) and 3 µl of freshly prepared 0.1 M sodium periodate solution. The reaction was incubated for 1 h in the dark at 4°C or room temperature. Following the incubation, the reaction was stopped by adding 4 µl of 10% ethylene glycol. Thereafter the mixture was incubated at room temperature for 15 minutes. After ethanol precipitation, the product was resuspended in 10µl or more of water or appropriate buffer and dialyzed against water.

15

Following exidation of the diel groups at the 5' ends of the mRNAs, the derivatized eligenucleotide was joined to the resulting aldehydes as described in Example 10.

### **EXAMPLE 10**

## Reaction of Aldehydes with Derivatized Oligonucleotides

The oxidized mRNA was dissolved in an acidic medium such as 50  $\mu$ l of sodium acetate pH 4-6. 50  $\mu$ l of a solution of the derivatized oligonucleotide was added such that an mRNA:derivatized oligonucleotide ratio of 1:20 was obtained and mixture was reduced with a borohydride. The mixture was allowed to incubate for 2 h at 37°C or overnight (14 h) at 10°C. The mixture was ethanol precipitated, resuspended in 10µl or more of water or appropriate buffer and dialyzed against distilled water. If desired, the resulting product may be analyzed using acrylamide gel 10 electrophoresis, HPLC analysis, or other conventional techniques.

Following the attachment of the derivatized oligonucleotide to the mRNAs, a reverse transcription reaction may be performed as described in Example 11 below.

#### **EXAMPLE 11**

## Reverse Transcription of mRNAs

An oligodeoxyribonucleotide was derivatized as follows. 3 OD units of an oligodeoxyribonucleotide of sequence ATCAAGAATTCGCACGAGACCATTA (SEQ ID NO:3) having 5'-OH and 3'-P ends were dissolved in 70 µl of a 1.5 M hydroxybenzotriazole solution, pH 5.3, prepared in dimethylformamide/water (75:25) containing 2 µg of 1-ethyl-3-(3dimethylaminopropyl)carbodiimide. The mixture was incubated for 2 h 30 min at 22°C. The mixture was then precipitated twice in LiClO<sub>4</sub>/acetone. The pellet was resuspended in 200 µl of 0.25 M hydrazine and incubated at 8°C 20 from 3 to 14 h. Following the hydrazine reaction, the mixture was precipitated twice in LiClO<sub>4</sub>/acetone.

The messenger RNAs to be reverse transcribed were extracted from blocks of placenta having sides of 2 cm which had been stored at -80°C. The mRNA was extracted using conventional acidic phenol techniques. Oligo-dT chromatography was used to purify the mRNAs. The integrity of the mRNAs was checked by Northern-blotting.

The diol groups on 7 µg of the placental mRNAs were oxidized as described above in Example 9. The 25 derivatized oligonucleotide was joined to the mRNAs as described in Example 10 above except that the precipitation step was replaced by an exclusion chromatography step to remove derivatized oligodeoxyribonucleotides which were not joined to mRNAs. Exclusion chromatography was performed as follows:

10 ml of AcA34 (BioSepra#230151) gel were equilibrated in 50 ml of a solution of 10 mM Tris pH 8.0, 300 mM NaCl, 1 mM EDTA, and 0.05% SDS. The mixture was allowed to sediment. The supernatant was eliminated and 30 the gel was resuspended in 50 ml of buffer. This procedure was repeated 2 or 3 times.

A glass bead (diameter 3 mm) was introduced into a 2 ml disposable pipette (length 25 cm). The pipette was filled with the gel suspension until the height of the gel stabilized at 1 cm from the top of the pipette. The column was then equilibrated with 20 ml of equilibration buffer (10 mM Tris HCl pH 7.4, 20 mM NaCl).

10  $\mu$ l of the mRNA which had been reacted with the derivatized oligonucleotide were mixed in 39  $\mu$ l of 10 mM urea and 2  $\mu$ l of blue-glycerol buffer, which had been prepared by dissolving 5 mg of bromophenol blue in 60% glycerol (v/v), and passing the mixture through a filter with a filter of diameter 0.45  $\mu$ m.

The column was loaded. As soon as the sample had penetrated, equilibration buffer was added. 100 µl fractions were collected. Derivatized oligonucleotide which had not been attached to mRNA appeared in fraction 16 and later fractions. Fractions 3 to 15 were combined and precipitated with ethanol.

The mRNAs which had been reacted with the derivatized oligonucleotide were spotted on a nylon membrane and hybridized to a radioactive probe using conventional techniques. The radioactive probe used in these hybridizations was an oligodeoxyribonucleotide of sequence TAATGGTCTCGTGCGAATTCTTGAT (SEQ ID NO:4) which was anticomplementary to the derivatized oligonucleotide and was labeled at its 5' end with <sup>32</sup>P. 1/10th of the mRNAs which had been reacted with the derivatized oligonucleotide was spotted in two spots on the membrane and the membrane was visualized by autoradiography after hybridization of the probe. A signal was observed, indicating that the derivatized oligonucleotide had been joined to the mRNA.

The remaining 9/10 of the mRNAs which had been reacted with the derivatized oligonucleotide was reverse transcribed as follows. A reverse transcription reaction was carried out with reverse transcriptase following the manufacturer's instructions. To prime the reaction, 50 pmol of nonamers with random sequence were used.

A portion of the resulting cDNA was spotted on a positively charged nylon membrane using conventional methods. The cDNAs were spotted on the membrane after the cDNA:RNA heteroduplexes had been subjected to an alkaline hydrolysis in order to eliminate the RNAs. An oligonucleotide having a sequence identical to that of the derivatized oligonucleotide was labeled at its 5' end with <sup>32</sup>P and hybridized to the cDNA blots using conventional techniques. Single-stranded cDNAs resulting from the reverse transcription reaction were spotted on the membrane. As controls, the blot contained 1 pmol, 100 fmol, 50 fmol, 10 fmol and 1 fmol respectively of a control oligodeoxyribonucleotide of sequence identical to that of the derivatized oligonucleotide. The signal observed in the spots containing the cDNA indicated that approximately 15 fmol of the derivatized oligonucleotide had been reverse transcribed.

These results demonstrate that the reverse transcription can be performed through the cap and, in particular, that reverse transcriptase crosses the 5'-P-P-P-5' bond of the cap of eukaryotic messenger RNAs.

The single stranded cDNAs obtained after the above first strand synthesis were used as template for PCR reactions. Two types of reactions were carried out. First, specific amplification of the mRNAs for the alpha globin, dehydrogenase, pp15 and elongation factor E4 were carried out using the following pairs of oligodeoxyribonucleotide primers.

### alpha-globin

30

GLO-S: CCG ACA AGA CCA ACG TCA AGG CCG C (SEQ ID NO:5)

GLO-As: TCA CCA GCA GGC AGT GGC TTA GGA G 3' (SEO ID NO:6)

dehydrogenase

3 DH-S: AGT GAT TCC TGC TAC TTT GGA TGG C (SEQ ID NO:7)

3 DH-As: GCT TGG TCT TGT TCT GGA GTT TAG A (SEQ ID NO:8)

pp15

PP15-S: TCC AGA ATG GGA GAC AAG CCA ATT T (SEQ ID NO:9)

5. PP15-As: AGG GAG GAG GAA ACA GCG TGA GTC C (SEO ID NO:10)

**Elongation factor E4** 

EFA1-S: ATG GGA AAG GAA AAG ACT CAT ATC A (SEQ ID NO:11)

EF1A-As: AGC AGC AAC AAT CAG GAC AGC ACA G (SEO ID NO:12)

Non specific amplifications were also carried out with the antisense (\_As) oligodeoxyribonucleotides of the pairs described above and a primer chosen from the sequence of the derivatized oligodeoxyribonucleotide (ATCAAGAATTCGCACGAGACCATTA) (SEQ ID NO:13).

A 1.5% agarose gel containing the following samples corresponding to the PCR products of reverse transcription was stained with ethidium bromide. (1/20th of the products of reverse transcription were used for each PCR reaction).

- Sample 1: The products of a PCR reaction using the globin primers of SEQ ID NOs 5 and 6 in the presence of cDNA.
  - Sample 2: The products of a PCR reaction using the globin primers of SEQ ID NOs 5 and 6 in the absence of added cDNA.
- Sample 3: The products of a PCR reaction using the dehydrogenase primers of SEQ ID NOs 7 and 8 in the presence of cDNA.
  - Sample 4: The products of a PCR reaction using the dehydrogenase primers of SEO ID NOs 7 and 8 in the absence of added cDNA.
  - Sample 5: The products of a PCR reaction using the pp15 primers of SEQ ID NOs 9 and 10 in the presence of cDNA.
- 25 Sample 6: The products of a PCR reaction using the pp15 primers of SEQ ID NOs 9 and 10 in the absence of added cDNA.
  - Sample 7: The products of a PCR reaction using the EIE4 primers of SEQ ID NOs 11 and 12 in the presence of added cDNA.
- Sample 8: The products of a PCR reaction using the EIE4 primers of SEQ ID NOs 11 and 12 in the absence of 30 added cDNA.
  - In Samples 1, 3, 5 and 7, a band of the size expected for the PCR product was observed, indicating the presence of the corresponding sequence in the cDNA population.

PCR reactions were also carried out with the antisense oligonucleotides of the globin and dehydrogenase primers (SEQ ID NOs 6 and 8) and an oligonucleotide whose sequence corresponds to that of the derivatized

oligonucleotide. The presence of PCR products of the expected size in the samples corresponding to samples 1 and 3 above indicated that the derivatized oligonucleotide had been incorporated.

The above examples summarize the chemical procedure for enriching mRNAs for those having intact 5' ends.

Further detail regarding the chemical approaches for obtaining mRNAs having intact 5' ends are disclosed in

International Application No. W096/34981, published November 7, 1996.

Strategies based on the above chemical modifications to the 5' cap structure may be utilized to generate cDNAs which have been selected to include the 5' ends of the mRNAs from which they are derived. In one version of such procedures, the 5' ends of the mRNAs are modified as described above. Thereafter, a reverse transcription reaction is conducted to extend a primer complementary to the mRNA to the 5' end of the mRNA. Single stranded RNAs are eliminated to obtain a population of cDNA/mRNA heteroduplexes in which the mRNA includes an intact 5' end. The resulting heteroduplexes may be captured on a solid phase coated with a molecule capable of interacting with the molecule used to derivatize the 5' end of the mRNA. Thereafter, the strands of the heteroduplexes are separated to recover single stranded first cDNA strands which include the 5' end of the mRNA. Second strand cDNA synthesis may then proceed using conventional techniques. For example, the procedures disclosed in WO 96/34981 or in Carninci, P. et al. High-Efficiency Full-Length cDNA Cloning by Biotinylated CAP Trapper. Genomics 37:327-336 (1996) may be employed to select cDNAs which include the sequence derived from the 5' end of the coding sequence of the mRNA.

Following ligation of the oligonucleotide tag to the 5' cap of the mRNA, a reverse transcription reaction is conducted to extend a primer complementary to the mRNA to the 5' end of the mRNA. Following elimination of the RNA component of the resulting heteroduplex using standard techniques, second strand cDNA synthesis is conducted with a primer complementary to the oligonucleotide tag.

Figure 1 summarizes the above procedures for obtaining cDNAs which have been selected to include the 5' ends of the mRNAs from which they are derived.

# B. Enzymatic Methods for Obtaining mRNAs having Intact 5' Ends

Other techniques for selecting cDNAs extending to the 5' end of the mRNA from which they are derived are

fully enzymatic. Some versions of these techniques are disclosed in Dumas Milne Edwards J.B. (Doctoral Thesis of Paris
VI University, Le clonage des ADNc complets: difficultes et perspectives nouvelles. Apports pour l'etude de la regulation
de l'expression de la tryptophane hydroxylase de rat, 20 Dec. 1993), EPO 625572 and Kato et al. Construction of a
Human Full-Length cDNA Bank. Gene 150:243-250 (1994).

Briefly, in such approaches, isolated mRNA is treated with alkaline phosphatase to remove the phosphate

groups present on the 5' ends of uncapped incomplete mRNAs. Following this procedure, the cap present on full length mRNAs is enzymatically removed with a decapping enzyme such as T4 polynucleotide kinase or tobacco acid pyrophosphatase. An oligonucleotide, which may be either a DNA oligonucleotide or a DNA-RNA hybrid oligonucleotide having RNA at its 3' end, is then ligated to the phosphate present at the 5' end of the decapped mRNA using T4 RNA

ligase. The oligonucleotide may include a restriction site to facilitate cloning of the cDNAs following their synthesis. Example 12 below describes one enzymatic method based on the doctoral thesis of Dumas.

## **EXAMPLE 12**

#### Enzymatic Approach for Obtaining 5' ESTs

Twenty micrograms of PolyA+ RNA were dephosphorylated using Calf Intestinal Phosphatase (Biolabs). After a phenol chloroform extraction, the cap structure of mRNA was hydrolysed using the Tobacco Acid Pyrophosphatase (purified as described by Shinshi et al., Biochemistry 15: 2185-2190, 1976) and a hemi 5'DNA/RNA-3' oligonucleotide having an unphosphorylated 5' end, a stretch of adenosine ribophosphate at the 3' end, and an EcoRI site near the 5' end was ligated to the 5'P ends of mRNA using the T4 RNA ligase (Biolabs). Oligonucleotides suitable for use in this 10 procedure are preferably 30-50 bases in length. Oligonucleotides having an unphosphorylated 5' end may be synthesized by adding a fluorochrome at the 5' end. The inclusion of a stretch of adenosine ribophosphates at the 3' end of the oligonucleotide increases ligation efficiency. It will be appreciated that the oligonucleotide may contain cloning sites other than EcoRI.

Following ligation of the oligonucleotide to the phosphate present at the 5' end of the decapped mRNA, first 15 and second strand cDNA synthesis may be carried out using conventional methods or those specified in EPO 625,572 and Kato et al. Construction of a Human Full-Length cDNA Bank, Gene 150:243-250 (1994), and Dumas Milne Edwards, supra. The resulting cDNA may then be ligated into vectors such as those disclosed in Kato et al. Construction of a Human Full-Length cDNA Bank. Gene 150:243-250 (1994) or other nucleic acid vectors known to those skilled in the art using techniques such as those described in Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold 20 Spring Harbor Laboratory Press, 1989.

## II. Characterization of 5' ESTs

The above chemical and enzymatic approaches for enriching mRNAs having intact 5' ends were employed to obtain 5' ESTs. First, mRNAs were prepared as described in Example 13 below.

#### **EXAMPLE 13**

25

5

## Preparation of mRNA

Total human RNAs or PolyA + RNAs derived from 29 different tissues were respectively purchased from LABIMO and CLONTECH and used to generate 44 cDNA libraries as described below. The purchased RNA had been isolated from cells or tissues using acid guanidium thiocyanate-phenol-chloroform extraction (Chomczyniski, P and Sacchi, N., Analytical Biochemistry 162:156-159, 1987). PolyA + RNA was isolated from total RNA (LABIMO) by 30 two passes of oligodT chromatography, as described by Aviv and Leder (Aviv, H. and Leder, P., Proc. Natl. Acad. Sci. USA 69:1408-1412, 1972) in order to eliminate ribosomal RNA.

The quality and the integrity of the poly A+ were checked. Northern blots hybridized with a globin probe were used to confirm that the mRNAs were not degraded. Contamination of the PolyA+ mRNAs by ribosomal sequences was checked using RNAs blots and a probe derived from the sequence of the 28S RNA. Preparations of mRNAs with less

than 5% of ribosomal RNAs were used in library construction. To avoid constructing libraries with RNAs contaminated by exogenous sequences (prokaryotic or fungal), the presence of bacterial 16S ribosomal sequences or of two highly expressed mRNAs was examined using PCR.

Following preparation of the mRNAs, the above described chemical and/or the enzymatic procedures for enriching mRNAs having intact 5' ends discussed above were employed to obtain 5' ESTs from various tissues. In both approaches an oligonucleotide tag was attached to the cap at the 5' ends of the mRNAs. The oligonucleotide tag had an EcoRI site therein to facilitate later cloning procedures.

Following attachment of the oligonucleotide tag to the mRNA by either the chemical or enzymatic methods, the integrity of the mRNA was examined by performing a Northern blot with 200-500ng of mRNA using a probe complementary to the oligonucleotide tag.

## **EXAMPLE 14**

# cDNA Synthesis Using mRNA Templates Having Intact 5' Ends

For the mRNAs joined to oligonucleotide tags using both the chemical and enzymatic methods, first strand cDNA synthesis was performed using reverse transcriptase with random nonamers as primers. In order to protect internal EcoRI sites in the cDNA from digestion at later steps in the procedure, methylated dCTP was used for first strand synthesis. After removal of RNA by an alkaline hydrolysis, the first strand of cDNA was precipitated using isopropanol in order to eliminate residual primers.

For both the chemical and the enzymatic methods, the second strand of the cDNA was synthesized with a Klenow fragment using a primer corresponding to the 5'end of the ligated oligonucleotide described in Example 12.

Preferably, the primer is 20-25 bases in length. Methylated dCTP was also used for second strand synthesis in order to protect internal EcoRI sites in the cDNA from digestion during the cloning process.

Following cDNA synthesis, the cDNAs were cloned into pBlueScript as described in Example 15 below.

#### **EXAMPLE 15**

## Insertion of cDNAs into BlueScript

Following second strand synthesis, the ends of the cDNA were blunted with T4 DNA polymerase (Biolabs) and the cDNA was digested with EcoRI. Since methylated dCTP was used during cDNA synthesis, the EcoRI site present in the tag was the only site which was hemi-methylated. Consequently, only the EcoRI site in the oligonucleotide tag was susceptible to EcoRI digestion. The cDNA was then size fractionated using exclusion chromatography (AcA, Biosepra). Fractions corresponding to cDNAs of more than 150 bp were pooled and ethanol precipitated. The cDNA was directionally cloned into the Smal and EcoRI ends of the phagemid pBlueScript vector (Stratagene). The ligation mixture was electroporated into bacteria and propagated under appropriate antibiotic selection.

Clones containing the oligonucleotide tag attached were selected as described in Example 16 below.

### **EXAMPLE 16**

Selection of Clones Having the Oligonucleotide Tag Attached Thereto

The plasmid DNAs containing 5' EST libraries made as described above were purified (Qiagen). A positive selection of the tagged clones was performed as follows. Briefly, in this selection procedure, the plasmid DNA was converted to single stranded DNA using gene II endonuclease of the phage F1 in combination with an exonuclease (Chang et al., Gene 127:95-8, 1993) such as exonuclease III or T7 gene 6 exonuclease. The resulting single stranded DNA was then purified using paramagnetic beads as described by Fry et al., Biotechniques, 13: 124-131, 1992. In this procedure, the single stranded DNA was hybridized with a biotinylated oligonucleotide having a sequence corresponding to the 3' end of the oligonucleotide described in Example 13. Preferably, the primer has a length of 20-25 bases. Clones including a sequence complementary to the biotinylated oligonucleotide were captured by incubation with streptavidin coated magnetic beads followed by magnetic selection. After capture of the positive clones, the plasmid DNA was released from the magnetic beads and converted into double stranded DNA using a DNA polymerase such as the ThermoSequenase obtained from Amersham Pharmacia Biotech. Alternatively, protocols such as the Gene Trapper kit (Gibco BRL) may be used. The double stranded DNA was then electroporated into bacteria. The percentage of positive clones having the 5' tag oligonucleotide was estimated to typically rank between 90 and 98% using dot blot analysis.

Following electroporation, the libraries were ordered in 384-microtiter plates (MTP). A copy of the MTP was stored for future needs. Then the libraries were transferred into 96 MTP and sequenced as described below.

## **EXAMPLE 17**

#### Sequencing of Inserts in Selected Clones

Plasmid inserts were first amplified by PCR on PE 9600 thermocyclers (Perkin-Elmer), using standard SETA-A and SETA-B primers (Genset SA), AmpliTaqGold (Perkin-Elmer), dNTPs (Boehringer), buffer and cycling conditions as recommended by the Perkin-Elmer Corporation.

PCR products were then sequenced using automatic ABI Prism 377 sequencers (Perkin Elmer, Applied
Biosystems Division, Foster City, CA). Sequencing reactions were performed using PE 9600 thermocyclers (Perkin Elmer)
with standard dye-primer chemistry and ThermoSequenase (Amersham Life Science). The primers used were either T7
or 21M13 (available from Genset SA) as appropriate. The primers were labeled with the JOE, FAM, ROX and TAMRA
dyes. The dNTPs and ddNTPs used in the sequencing reactions were purchased from Boehringer. Sequencing buffer,
reagent concentrations and cycling conditions were as recommended by Amersham.

Following the sequencing reaction, the samples were precipitated with EtOH, resuspended in formamide loading buffer, and loaded on a standard 4% acrylamide gel. Electrophoresis was performed for 2.5 hours at 3000V on an ABI 377 sequencer, and the sequence data were collected and analyzed using the ABI Prism DNA Sequencing Analysis Software, version 2.1.2.

The sequence data from the 44 cDNA libraries made as described above were transferred to a proprietary database, where quality control and validation steps were performed. A proprietary base-caller ("Trace"), working using a Unix system automatically flagged suspect peaks, taking into account the shape of the peaks, the inter-peak resolution, and the noise level. The proprietary base-caller also performed an automatic trimming. Any stretch of 25 or

fewer bases having more than 4 suspect peaks was considered unreliable and was discarded. Sequences corresponding to cloning vector or ligation oligonucleotides were automatically removed from the EST sequences. However, the resulting EST sequences may contain 1 to 5 bases belonging to the above mentioned sequences at their 5' end. If needed, these can easily be removed on a case by case basis.

Thereafter, the sequences were transferred to the proprietary NETGENE™ Database for further analysis as described below.

Following sequencing as described above, the sequences of the 5' ESTs were entered in a proprietary database called NETGENETM for storage and manipulation. It will be appreciated by those skilled in the art that the data could be stored and manipulated on any medium which can be read and accessed by a computer. Computer readable media include magnetically readable media, optically readable media, or electronically readable media. For example, the computer readable media may be a hard disc, a floppy disc, a magnetic tape, CD-ROM, RAM, or ROM as well as other types of other media known to those skilled in the art.

In addition, the sequence data may be stored and manipulated in a variety of data processor programs in a variety of formats. For example, the sequence data may be stored as text in a word processing file, such as

15 MicrosoftWORD or WORDPERFECT or as an ASCII file in a variety of database programs familiar to those of skill in the art, such as DB2, SYBASE, or ORACLE.

The computer readable media on which the sequence information is stored may be in a personal computer, a network, a server or other computer systems known to those skilled in the art. The computer or other system preferably includes the storage media described above, and a processor for accessing and manipulating the sequence data.

Once the sequence data has been stored it may be manipulated and searched to locate those stored sequences which contain a desired nucleic acid sequence or which encode a protein having a particular functional domain. For example, the stored sequence information may be compared to other known sequences to identify homologies, motifs implicated in biological function, or structural motifs.

Programs which may be used to search or compare the stored sequences include the MacPattern (EMBL),

25 BLAST, and BLAST2 program series (NCBI), basic local alignment search tool programs for nucleotide (BLASTN) and
peptide (BLASTX) comparisons (Altschul et al, J. Mol. Biol. 215: 403 (1990)) and FASTA (Pearson and Lipman, Proc.

Natl. Acad. Sci. USA, 85: 2444 (1988)). The BLAST programs then extend the alignments on the basis of defined
match and mismatch criteria.

Motifs which may be detected using the above programs include sequences encoding leucine zippers, helix-turnhelix motifs, glycosylation sites, ubiquitination sites, alpha helices, and beta sheets, signal sequences encoding signal peptides which direct the secretion of the encoded proteins, sequences implicated in transcription regulation such as homeoboxes, acidic stretches, enzymatic active sites, substrate binding sites, and enzymatic cleavage sites.

25

Before searching the cDNAs in the NETGENETM database for sequence motifs of interest, cDNAs derived from mRNAs which were not of interest were identified and eliminated from further consideration as described in Example 18 below.

### **EXAMPLE 18**

#### Elimination of Undesired Sequences from Further Consideration

5' ESTs in the NETGENE™ database which were derived from undesired sequences such as transfer RNAs, ribosomal RNAs, mitochondrial RNAs, procaryotic RNAs, fungal RNAs, Alu sequences, L1 sequences, or repeat sequences were identified using the FASTA and BLASTN programs with the parameters listed in Table II.

To eliminate 5' ESTs encoding tRNAs from further consideration, the 5' EST sequences were compared to the 10 sequences of 1190 known tRNAs obtained from EMBL release 38, of which 100 were human. The comparison was performed using FASTA on both strands of the 5' ESTs. Sequences having more than 80% homology over more than 60 nucleotides were identified as tRNA. Of the 144,341 sequences screened, 26 were identified as tRNAs and eliminated from further consideration.

To eliminate 5' ESTs encoding rRNAs from further consideration, the 5' EST sequences were compared to the 15, sequences of 2497 known rRNAs obtained from EMBL release 38, of which 73 were human. The comparison was performed using BLASTN on both strands of the 5' ESTs with the parameter S = 108. Sequences having more than 80% homology over stretches longer than 40 nucleotides were identified as rRNAs. Of the 144,341 sequences screened, 3.312 were identified as rRNAs and eliminated from further consideration.

To eliminate 5' ESTs encoding mtRNAs from further consideration, the 5' EST sequences were compared to 20 the sequences of the two known mitochondrial genomes for which the entire genomic sequences are available and all sequences transcribed from these mitochondrial genomes including tRNAs, rRNAs, and mRNAs for a total of 38 sequences. The comparison was performed using BLASTN on both strands of the 5' ESTs with the parameter S = 108. Sequences having more than 80% homology over stretches longer than 40 nucleotides were identified as mtRNAs. Of the 144,341 sequences screened, 6,110 were identified as mtRNAs and eliminated from further consideration.

Sequences which might have resulted from exogenous contaminants were eliminated from further consideration by comparing the 5' EST sequences to release 46 of the EMBL bacterial and fungal divisions using BLASTN with the parameter S = 144. All sequences having more than 90% homology over at least 40 nucleotides were identified as exogenous contaminants. Of the 42 cDNA libraries examined, the average percentages of procaryotic and fungal sequences contained therein were 0.2% and 0.5% respectively. Among these sequences, only one could be 30 identified as a sequence specific to fungi. The others were either fungal or procaryotic sequences having homologies with vertebrate sequences or including repeat sequences which had not been masked during the electronic comparison.

In addition, the 5' ESTs were compared to 6093 Alu sequences and 1115 L1 sequences to mask 5' ESTs containing such repeat sequences from further consideration. 5' ESTs including THE and MER repeats, SSTR sequences or satellite, micro-satellite, or telomeric repeats were also eliminated from further consideration. On average, 11.5% of

the sequences in the libraries contained repeat sequences. Of this 11.5%, 7% contained Alu repeats, 3.3% contained L1 repeats and the remaining 1.2% were derived from the other types of repetitive sequences which were screened. These percentages are consistent with those found in cDNA libraries prepared by other groups. For example, the cDNA libraries of Adams et al. contained between 0% and 7.4% Alu repeats depending on the source of the RNA which was used to prepare the cDNA library (Adams et al., *Nature* 377:174, 1996).

The sequences of those 5' ESTs remaining after the elimination of undesirable sequences were compared with the sequences of known human mRNAs to determine the accuracy of the sequencing procedures described above.

### **EXAMPLE 19**

# Measurement of Sequencing Accuracy by Comparison to Known Sequences

To further determine the accuracy of the sequencing procedure described above, the sequences of 5' ESTs derived from known sequences were identified and compared to the known sequences. First, a FASTA analysis with overhangs shorter than 5 bp on both ends was conducted on the 5' ESTs to identify those matching an entry in the public human mRNA database. The 6655 5' ESTs which matched a known human mRNA were then realigned with their cognate mRNA and dynamic programming was used to include substitutions, insertions, and deletions in the list of "errors" which would be recognized. Errors occurring in the last 10 bases of the 5' EST sequences were ignored to avoid the inclusion of spurious cloning sites in the analysis of sequencing accuracy.

This analysis revealed that the sequences incorporated in the NETGENE™ database had an accuracy of more than 99.5%.

To determine the efficiency with which the above selection procedures select cDNAs which include the 5' ends of their corresponding mRNAs, the following analysis was performed.

## **EXAMPLE 20**

# Determination of Efficiency of 5' EST Selection

To determine the efficiency at which the above selection procedures isolated 5' ESTs which included sequences close to the 5' end of the mRNAs from which they were derived, the sequences of the ends of the 5' ESTs which were derived from the elongation factor 1 subunit  $\alpha$  and ferritin heavy chain genes were compared to the known cDNA sequences for these genes. Since the transcription start sites for the elongation factor 1 subunit  $\alpha$  and ferritin heavy chain are well characterized, they may be used to determine the percentage of 5' ESTs derived from these genes which included the authentic transcription start sites.

For both genes, more than 95% of the cDNAs included sequences close to or upstream of the 5' end of the corresponding mRNAs.

To extend the analysis of the reliability of the procedures for isolating 5' ESTs from ESTs in the NETGENETM database, a similar analysis was conducted using a database composed of human mRNA sequences extracted from GenBank database release 97 for comparison. For those 5' ESTs derived from mRNAs included in the GeneBank database, more than 85% had their 5' ends close to the 5' ends of the known sequence. As some of the mRNA

sequences available in the GenBank database are deduced from genomic sequences, a 5' end matching with these sequences will be counted as an internal match. Thus, the method used here underestimates the yield of ESTs including the authentic 5' ends of their corresponding mRNAs.

The EST libraries made above included multiple 5' ESTs derived from the same mRNA. The sequences of such 5' ESTs were compared to one another and the longest 5' ESTs for each mRNA were identified. Overlapping cDNAs were assembled into continuous sequences (contigs). The resulting continuous sequences were then compared to public databases to gauge their similarity to known sequences, as described in Example 21 below.

### **EXAMPLE 21**

## Clustering of the 5' ESTs and Calculation of Novelty Indices for cDNA Libraries

For each sequenced EST library, the sequences were clustered by the 5' end. Each sequence in the library was compared to the others with BLASTN2 (direct strand, parameters S = 107). ESTs with High Scoring Segment Pairs (HSPs) at least 25 bp long, having 95% identical bases and beginning closer than 10 bp from each EST 5' end were grouped. The longest sequence found in the cluster was used as representative of the cluster. A global clustering between libraries was then performed leading to the definition of super-contigs.

To assess the yield of new sequences within the EST libraries, a novelty rate (NR) was defined as: NR = 100 X (Number of new unique sequences found in the library/Total number of sequences from the library). Typically, novelty rating range between 10% and 41% depending on the tissue from which the EST library was obtained. For most of the libraries, the random sequencing of 5' EST libraries was pursued until the novelty rate reached 20%.

Following characterization as described above, the collection of 5' ESTs in NETGENE<sup>TM</sup> was screened to 20 identify those 5' ESTs bearing potential signal sequences as described in Example 22 below.

#### **EXAMPLE 22**

## Identification of Potential Signal Sequences in 5' ESTs

The 5' ESTs in the NETGENETM database were screened to identify those having an uninterrupted open reading frame (ORF) longer than 45 nucleotides beginning with an ATG codon and extending to the end of the EST.

25 Approximately half of the cDNA sequences in NETGENETM contained such an ORF. The ORFs of these 5' ESTs were searched to identify potential signal motifs using slight modifications of the procedures disclosed in Von Heijne, G. A New Method for Predicting Signal Sequence Cleavage Sites. Nucleic Acids Res. 14:4683-4690 (1986). Those 5' EST sequences encoding a 15 amino acid long stretch with a score of at least 3.5 in the Von Heijne signal peptide identification matrix were considered to possess a signal sequence. Those 5' ESTs which matched a known human mRNA or EST sequence and had a 5' end more than 20 nucleotides downstream of the known 5' end were excluded from further analysis. The remaining cDNAs having signal sequences therein were included in a database called SIGNALTAGTM.

To confirm the accuracy of the above method for identifying signal sequences, the analysis of Example 23 was performed.

#### **EXAMPLE 23**

# Confirmation of Accuracy of Identification of Potential Signal Sequences in 5' ESTs

The accuracy of the above procedure for identifying signal sequences encoding signal peptides was evaluated by applying the method to the 43 amino terminal amino acids of all human SwissProt proteins. The computed Von Heijne score for each protein was compared with the known characterization of the protein as being a secreted protein or a non-secreted protein. In this manner, the number of non-secreted proteins having a score higher than 3.5 (false positives) and the number of secreted proteins having a score lower than 3.5 (false negatives) could be calculated.

Using the results of the above analysis, the probability that a peptide encoded by the 5' region of the mRNA is in fact a genuine signal peptide based on its Von Heijne's score was calculated based on either the assumption that 10% of human proteins are secreted or the assumption that 20% of human proteins are secreted. The results of this analysis are shown in Figures 2 and 3.

Using the above method of identifying secretory proteins, 5' ESTs for human glucagon, gamma interferon induced monokine precursor, secreted cyclophilin-like protein, human pleiotropin, and human biotinidase precursor all of which are polypeptides which are known to be secreted, were obtained. Thus, the above method successfully identified those 5' ESTs which encode a signal peptide.

To confirm that the signal peptide encoded by the 5' ESTs actually functions as a signal peptide, the signal sequences from the 5' ESTs may be cloned into a vector designed for the identification of signal peptides. Some signal peptide identification vectors are designed to confer the ability to grow in selective medium on host cells which have a signal sequence operably inserted into the vector. For example, to confirm that a 5' EST encodes a genuine signal peptide, the signal sequence of the 5' EST may be inserted upstream and in frame with a non-secreted form of the yeast invertase gene in signal peptide selection vectors such as those described in U.S. Patent No. 5,536,637. Growth of host cells containing signal sequence selection vectors having the signal sequence from the 5' EST inserted therein confirms that the 5' EST encodes a genuine signal peptide.

Alternatively, the presence of a signal peptide may be confirmed by cloning the extended cDNAs obtained using
the ESTs into expression vectors such as pXT1 (as described below), or by constructing promoter-signal sequencereporter gene vectors which encode fusion proteins between the signal peptide and an assayable reporter protein. After
introduction of these vectors into a suitable host cell, such as COS cells or NIH 3T3 cells, the growth medium may be
harvested and analyzed for the presence of the secreted protein. The medium from these cells is compared to the
medium from cells containing vectors lacking the signal sequence or extended cDNA insert to identify vectors which
encode a functional signal peptide or an authentic secreted protein.

Those 5' ESTs which encoded a signal peptide, as determined by the method of Example 22 above, were further grouped into four categories based on their homology to known sequences. The categorization of the 5' ESTs is described in Example 24 below.

## Categorization of 5' ESTs Encoding a Signal Peptide

Those 5' ESTs having a sequence not matching any known vertebrate sequence nor any publicly available EST sequence were designated "new." Of the sequences in the SIGNALTAG<sup>TM</sup> database, 947 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those 5' ESTs having a sequence not matching any vertebrate sequence but matching a publicly known EST were designated "EST-ext", provided that the known EST sequence was extended by at least 40 nucleotides in the 5' direction. Of the sequences in the SIGNALTAG<sup>TM</sup> database, 150 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those ESTs not matching any vertebrate sequence but matching a publicly known EST without extending the known EST by at least 40 nucleotides in the 5' direction were designated "EST." Of the sequences in the SIGNALTAG<sup>TM</sup> database, 599 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category.

Those 5' ESTs matching a human mRNA sequence but extending the known sequence by at least 40 nucleotides in the 5' direction were designated "VERT-ext." Of the sequences in the SIGNALTAGTM database, 23 of the 5' ESTs having a Von Heijne's score of at least 3.5 fell into this category. Included in this category was a 5' EST which extended the known sequence of the human translocase mRNA by more than 200 bases in the 5' direction. A 5' EST which extended the sequence of a human tumor suppressor gene in the 5' direction was also identified.

Figure 4 shows the distribution of 5' ESTs in each category and the number of 5' ESTs in each category having a given minimum von Heijne's score.

Each of the 5' ESTs was categorized based on the tissue from which its corresponding mRNA was obtained, 20 as described below in Example 25.

## **EXAMPLE 25**

## Categorization of Expression Patterns

Figure 5 shows the tissues from which the mRNAs corresponding to the 5' ESTs in each of the above described categories were obtained.

In addition to categorizing the 5' ESTs by the tissue from which the cDNA library in which they were first identified was obtained, the spatial and temporal expression patterns of the mRNAs corresponding to the 5' ESTs, as well as their expression levels, may be determined as described in Example 26 below. Characterization of the spatial and temporal expression patterns and expression levels of these mRNAs is useful for constructing expression vectors capable of producing a desired level of gene product in a desired spatial or temporal manner, as will be discussed in more detail 30 below.

In addition, 5' ESTs whose corresponding mRNAs are associated with disease states may also be identified. For example, a particular disease may result from lack of expression, over expression, or under expression of an mRNA corresponding to a 5' EST. By comparing mRNA expression patterns and quantities in samples taken from healthy

Sein.

individuals with those from individuals suffering from a particular disease, 5' ESTs responsible for the disease may be identified.

It will be appreciated that the results of the above characterization procedures for 5' ESTs also apply to extended cDNAs (obtainable as described below) which contain sequences adjacent to the 5' ESTs. It will also be appreciated that if it is desired to defer characterization until extended cDNAs have been obtained rather than characterizing the ESTs themselves, the above characterization procedures can be applied to characterize the extended cDNAs after their isolation.

### **EXAMPLE 26**

# Evaluation of Expression Levels and Patterns of mRNAs

10

# Corresponding to 5' ESTs or Extended cDNAs

Expression levels and patterns of mRNAs corresponding to 5' ESTs or extended cDNAs (obtainable as described below) may be analyzed by solution hybridization with long probes as described in International Patent Application No. WO 97/05277. Briefly, a 5' EST, extended cDNA, or fragment thereof corresponding to the gene encoding the mRNA to be characterized is inserted at a cloning site immediately downstream of a bacteriophage (T3, T7 or SP6) RNA polymerase promoter to produce antisense RNA. Preferably, the 5' EST or extended cDNA has 100 or more nucleotides. The plasmid is linearized and transcribed in the presence of ribonucleotides comprising modified ribonucleotides (i.e. biotin-UTP and DIG-UTP). An excess of this doubly labeled RNA is hybridized in solution with mRNA isolated from cells or tissues of interest. The hybridizations are performed under standard stringent conditions (40-50°C for 16 hours in an 80% formamide, 0.4 M NaCl buffer, pH 7-8). The unhybridized probe is removed by digestion with ribonucleases specific for single-stranded RNA (i.e. RNases CL3, T1, Phy M, U2 or A). The presence of the biotin-UTP modification enables capture of the hybrid on a microtitration plate coated with streptavidin. The presence of the DIG modification enables the hybrid to be detected and quantified by ELISA using an anti-DIG antibody coupled to alkaline phosphatase.

The 5' ESTs, extended cDNAs, or fragments thereof may also be tagged with nucleotide sequences for the serial analysis of gene expression (SAGE) as disclosed in UK Patent Application No. 2 305 241 A. In this method, cDNAs are prepared from a cell, tissue, organism or other source of nucleic acid for which it is desired to determine gene expression patterns. The resulting cDNAs are separated into two pools. The cDNAs in each pool are cleaved with a first restriction endonuclease, called an "anchoring enzyme," having a recognition site which is likely to be present at least once in most cDNAs. The fragments which contain the 5' or 3' most region of the cleaved cDNA are isolated by binding to a capture medium such as streptavidin coated beads. A first oligonucleotide linker having a first sequence for hybridization of an amplification primer and an internal restriction site for a "tagging endonuclease" is ligated to the digested cDNAs in the first pool. Digestion with the second endonuclease produces short "tag" fragments from the cDNAs.

25

A second oligonucleotide having a second sequence for hybridization of an amplification primer and an internal restriction site is ligated to the digested cDNAs in the second pool. The cDNA fragments in the second pool are also digested with the "tagging endonuclease" to generate short "tag" fragments derived from the cDNAs in the second pool. The "tags" resulting from digestion of the first and second pools with the anchoring enzyme and the tagging 5 endonuclease are ligated to one another to produce "ditags." In some embodiments, the ditags are concatamerized to produce ligation products containing from 2 to 200 ditags. The tag sequences are then determined and compared to the sequences of the 5' ESTs or extended cDNAs to determine which 5' ESTs or extended cDNAs are expressed in the cell, tissue, organism, or other source of nucleic acids from which the tags were derived. In this way, the expression pattern of the 5' ESTs or extended cDNAs in the cell, tissue, organism, or other source of nucleic acids is obtained.

Quantitative analysis of gene expression may also be performed using arrays. As used herein, the term array means a one dimensional, two dimensional, or multidimensional arrangement of full length cDNAs (i.e. extended cDNAs which include the coding sequence for the signal peptide, the coding sequence for the mature protein, and a stop codon), extended cDNAs, 5' ESTs or fragments of the full length cDNAs, extended cDNAs, or 5' ESTs of sufficient length to permit specific detection of gene expression. Preferably, the fragments are at least 15 nucleotides in length. More preferably, the fragments are at least 100 nucleotides in length. More preferably, the fragments are more than 100 nucleotides in length. In some embodiments the fragments may be more than 500 nucleotides in length.

For example, quantitative analysis of gene expression may be performed with full length cDNAs, extended cDNAs, 5' ESTs, or fragments thereof in a complementary DNA microarray as described by Schena et al. (Science 270:467-470, 1995; Proc. Natl. Acad. Sci. U.S.A. 93:10614-10619, 1996). Full length cDNAs, extended cDNAs, 5' 20 ESTs or fragments thereof are amplified by PCR and arrayed from 96-well microtiter plates onto silylated microscope slides using high-speed robotics. Printed arrays are incubated in a humid chamber to allow rehydration of the array elements and rinsed, once in 0.2% SDS for 1 min, twice in water for 1 min and once for 5 min in sodium borohydride solution. The arrays are submerged in water for 2 min at 95°C, transferred into 0.2% SDS for 1 min, rinsed twice with water, air dried and stored in the dark at 25°C.

Cell or tissue mRNA is isolated or commercially obtained and probes are prepared by a single round of reverse transcription. Probes are hybridized to 1 cm² microarrays under a 14 x 14 mm glass coverslip for 6-12 hours at 60°C. Arrays are washed for 5 min at 25°C in low stringency wash buffer (1 x SSC/0.2% SDS), then for 10 min at room temperature in high stringency wash buffer (0.1 x SSC/0.2% SDS). Arrays are scanned in 0.1 x SSC using a fluorescence laser scanning device fitted with a custom filter set. Accurate differential expression measurements are 30 obtained by taking the average of the ratios of two independent hybridizations.

Quantitative analysis of the expression of genes may also be performed with full length cDNAs, extended cDNAs, 5' ESTs, or fragments thereof in complementary DNA arrays as described by Pietu et al. (Genome Research 6:492-503, 1996). The full length cDNAs, extended cDNAs, 5' ESTs or fragments thereof are PCR amplified and spotted on membranes. Then, mRNAs originating from various tissues or cells are labeled with radioactive nucleotides.

After hybridization and washing in controlled conditions, the hybridized mRNAs are detected by phospho-imaging or autoradiography. Duplicate experiments are performed and a quantitative analysis of differentially expressed mRNAs is then performed.

Alternatively, expression analysis of the 5' ESTs or extended cDNAs can be done through high density

nucleotide arrays as described by Lockhart et al. (Nature Biotechnology 14: 1675-1680, 1996) and Sosnowsky et al.

(Proc. Natl. Acad. Sci. 94:1119-1123, 1997). Oligonucleotides of 15-50 nucleotides corresponding to sequences of the 5' ESTs or extended cDNAs are synthesized directly on the chip (Lockhart et al., supra) or synthesized and then addressed to the chip (Sosnowski et al., supra). Preferably, the oligonucleotides are about 20 nucleotides in length.

cDNA probes labeled with an appropriate compound, such as biotin, digoxigenin or fluorescent dye, are
synthesized from the appropriate mRNA population and then randomly fragmented to an average size of 50 to 100 nucleotides. The said probes are then hybridized to the chip. After washing as described in Lockhart et al., supra and application of different electric fields (Sosnowsky et al., Proc. Natl. Acad. Sci. 94:1119-1123)., the dyes or labeling compounds are detected and quantified. Duplicate hybridizations are performed. Comparative analysis of the intensity of the signal originating from cDNA probes on the same target oligonucleotide in different cDNA samples indicates a differential expression of the mRNA corresponding to the 5' EST or extended cDNA from which the oligonucleotide sequence has been designed.

# III. Use of 5' ESTs to Clone Extended cDNAs and to Clone the Corresponding Genomic DNAs

Once 5' ESTs which include the 5' end of the corresponding mRNAs have been selected using the procedures described above, they can be utilized to isolate extended cDNAs which contain sequences adjacent to the 5' ESTs. The extended cDNAs may include the entire coding sequence of the protein encoded by the corresponding mRNA, including the authentic translation start site, the signal sequence, and the sequence encoding the mature protein remaining after cleavage of the signal peptide. Such extended cDNAs are referred to herein as "full length cDNAs." Alternatively, the extended cDNAs may include only the sequence encoding the mature protein remaining after cleavage of the signal peptide, or only the sequence encoding the signal peptide.

Example 27 below describes a general method for obtaining extended cDNAs. Example 28 below describes the cloning and sequencing of several extended cDNAs, including extended cDNAs which include the entire coding sequence and authentic 5' end of the corresponding mRNA for several secreted proteins.

The methods of Examples 27, 28, and 29 can also be used to obtain extended cDNAs which encode less than the entire coding sequence of the secreted proteins encoded by the genes corresponding to the 5' ESTs. In some ambodiments, the extended cDNAs isolated using these methods encode at least 10 amino acids of one of the proteins encoded by the sequences of SEQ ID NOs: 40-140 and 242-377. In further embodiments, the extended cDNAs encode at least 20 amino acids of the proteins encoded by the sequences of SEQ ID NOs: 40-140 and 242-377. In further embodiments, the extended cDNAs encode at least 30 amino acids of the sequences of SEQ ID NOs: 40-140 and

242-377. In a preferred embodiment, the extended cDNAs encode a full length protein sequence, which includes the protein coding sequences of SEO ID NOs: 40-140 and 242-377.

### **EXAMPLE 27**

## General Method for Using 5' ESTs to Clone and Sequence Extended cDNAs

The following general method has been used to quickly and efficiently isolate extended cDNAs including sequence adjacent to the sequences of the 5' ESTs used to obtain them. This method may be applied to obtain extended cDNAs for any 5' EST in the NETGENE<sup>TM</sup> database, including those 5' ESTs encoding secreted proteins. The method is summarized in Figure 6.

## 1. Obtaining Extended cDNAs

#### 10 a) First strand synthesis

5

The method takes advantage of the known 5' sequence of the mRNA. A reverse transcription reaction is conducted on purified mRNA with a poly 14dT primer containing a 49 nucleotide sequence at its 5' end allowing the addition of a known sequence at the end of the cDNA which corresponds to the 3' end of the mRNA. For example, the primer may have the following sequence: 5'-ATC GTT GAG ACT CGT ACC AGC AGA GTC ACG AGA GAG ACT ACA CGG TAC TGG TTT TTT TTT TTT TTVN -3' (SEQ ID NO:14). Those skilled in the art will appreciate that other sequences may also be added to the poly dT sequence and used to prime the first strand synthesis. Using this primer and a reverse transcriptase such as the Superscript II (Gibco BRL) or Rnase H Minus M-MLV (Promega) enzyme, a reverse transcript anchored at the 3' polyA site of the RNAs is generated.

After removal of the mRNA hybridized to the first cDNA strand by alkaline hydrolysis, the products of the alkaline hydrolysis and the residual poly dT primer are eliminated with an exclusion column such as an AcA34 (Biosepra) matrix as explained in Example 11.

#### b) Second strand synthesis

30

A pair of nested primers on each end is designed based on the known 5' sequence from the 5' EST and the known 3' end added by the poly dT primer used in the first strand synthesis. Software used to design primers are either based on GC content and melting temperatures of oligonucleotides, such as OSP (Illier and Green, *PCR Meth. Appl.* 1:124-128, 1991), or based on the octamer frequency disparity method (Griffais et al., *Nucleic Acids Res.* 19: 3887-3891, 1991 such as PC-Rare (http://bioinformatics.weizmann.ac.il/software/PC-Rare/doc/manuel.html).

Preferably, the nested primers at the 5' end are separated from one another by four to nine bases. The 5' primer sequences may be selected to have melting temperatures and specificities suitable for use in PCR.

Preferably, the nested primers at the 3' end are separated from one another by four to nine bases. For example, the nested 3' primers may have the following sequences: (5'- CCA GCA GAG TCA CGA GAG AGA CTA CAC GG-3'(SEQ ID NO:15), and 5'- CAC GAG AGA GAC TAC ACG GTA CTG G-3' (SEQ ID NO:16). These primers were selected because they have melting temperatures and specificities compatible with their use in PCR. However, those skilled in the art will appreciate that other sequences may also be used as primers.

The first PCR run of 25 cycles is performed using the Advantage Tth Polymerase Mix (Clontech) and the outer primer from each of the nested pairs. A second 20 cycle PCR using the same enzyme and the inner primer from each of the nested pairs is then performed on 1/2500 of the first PCR product. Thereafter, the primers and nucleotides are removed.

# 5 2. Sequencing of Full Length Extended cDNAs or Fragments Thereof

Due to the lack of position constraints on the design of 5' nested primers compatible for PCR use using the DSP software, amplicons of two types are obtained. Preferably, the second 5' primer is located upstream of the translation initiation codon thus yielding a nested PCR product containing the whole coding sequence. Such a full length extended cDNA undergoes a direct cloning procedure as described in section a below. However, in some cases, the second 5' primer is located downstream of the translation initiation codon, thereby yielding a PCR product containing only part of the ORF. Such incomplete PCR products are submitted to a modified procedure described in section b below.

# a) Nested PCR products containing complete ORFs

When the resulting nested PCR product contains the complete coding sequence, as predicted from the 5'EST sequence, it is cloned in an appropriate vector such as pED6dpc2, as described in section 3.

## b) Nested PCR products containing incomplete ORFs

When the amplicon does not contain the complete coding sequence, intermediate steps are necessary to obtain both the complete coding sequence and a PCR product containing the full coding sequence. The complete coding sequence can be assembled from several partial sequences determined directly from different PCR products as described in the following section.

Once the full coding sequence has been completely determined, new primers compatible for PCR use are designed to obtain amplicons containing the whole coding region. However, in such cases, 3' primers compatible for PCR use are located inside the 3' UTR of the corresponding mRNA, thus yielding amplicons which lack part of this region, i.e. the polyA tract and sometimes the polyadenylation signal, as illustrated in figure 6. Such full length extended cDNAs are then cloned into an appropriate vector as described in section 3.

## c) Sequencing extended cDNAs

Sequencing of extended cDNAs is performed using a Die Terminator approach with the AmpliTaq DNA polymerase FS kit available from Perkin Elmer.

In order to sequence PCR fragments, primer walking is performed using software such as OSP to choose

30 primers and automated computer software such as ASMG (Sutton et al., *Genome Science Technol.* 1: 9-19, 1995) to construct contigs of walking sequences including the initial 5' tag using minimum overlaps of 32 nucleotides. Preferably, primer walking is performed until the sequences of full length cDNAs are obtained.

Completion of the sequencing of a given extended cDNA fragment is assessed as follows. Since sequences located after a polyA tract are difficult to determine precisely in the case of uncloned products, sequencing and primer

walking processes for PCR products are interrupted when a polyA tract is identified in extended cDNAs obtained as described in case b. The sequence length is compared to the size of the nested PCR product obtained as described above. Due to the limited accuracy of the determination of the PCR product size by gel electrophoresis, a sequence is considered complete if the size of the obtained sequence is at least 70 % the size of the first nested PCR product. If the length of the sequence determined from the computer analysis is not at least 70% of the length of the nested PCR product, these PCR products are cloned and the sequence of the insertion is determined. When Northern blot data are available, the size of the mRNA detected for a given PCR product is used to finally assess that the sequence is complete. Sequences which do not fulfill the above criteria are discarded and will undergo a new isolation procedure.

Sequence data of all extended cDNAs are then transferred to a proprietary database, where quality controls 10 and validation steps are carried out as described in example 15.

#### 3. Cloning of Full Length Extended cDNAs

20

The PCR product containing the full coding sequence is then cloned in an appropriate vector. For example, the extended cDNAs can be cloned into the expression vector pED6dpc2 (DiscoverEase, Genetics Institute, Cambridge, MA) as follows. The structure of pED6dpc2 is shown in Figure 7. pED6dpc2 vector DNA is prepared with blunt ends by performing an EcoRI digestion followed by a fill in reaction. The blunt ended vector is dephosphorylated. After removal of PCR primers and ethanol precipitation, the PCR product containing the full coding sequence or the extended cDNA obtained as described above is phosphorylated with a kinase subsequently removed by phenol-Sevag extraction and precipitation. The double stranded extended cDNA is then ligated to the vector and the resulting expression plasmid introduced into appropriate host cells.

Since the PCR products obtained as described above are blunt ended molecules that can be cloned in either direction, the orientation of several clones for each PCR product is determined. Then, 4 to 10 clones are ordered in microtiter plates and subjected to a PCR reaction using a first primer located in the vector close to the cloning site and a second primer located in the portion of the extended cDNA corresponding to the 3' end of the mRNA. This second primer may be the antisense primer used in anchored PCR in the case of direct cloning (case a) or the antisense primer located 25 inside the 3'UTR in the case of indirect cloning (case b). Clones in which the start codon of the extended cDNA is operably linked to the promoter in the vector so as to permit expression of the protein encoded by the extended cDNA are conserved and sequenced. In addition to the ends of cDNA inserts, approximately 50 bp of vector DNA on each side of the cDNA insert are also sequenced.

The cloned PCR products are then entirely sequenced according to the aforementioned procedure. In this case, 30 contig assembly of long fragments is then performed on walking sequences that have already contigated for uncloned PCR products during primer walking. Sequencing of cloned amplicons is complete when the resulting contigs include the whole coding region as well as overlapping sequences with vector DNA on both ends.

### 4. Computer Analysis of Full Length Extended cDNA

Sequences of all full length extended cDNAs are then submitted to further analysis as described below and using the parameters found in Table II with the following modifications. For screening of miscellaneous subdivisions of Genbank, FASTA was used instead of BLASTN and 15 nucleotide of homology was the limit instead of 17. For Alu detection, BLASTN was used with the following parameters: S = 72; identity = 70%; and length = 40 nucleotides.

- Polyadenylation signal and polyA tail which were not search for the 5' ESTs were searched. For polyadenylation signal detection the signal (AATAAA) was searched with one permissible mismatch in the last ten nucleotides preceding the 5' end of the polyA. For the polyA, a stretch of 8 amino acids in the last 20 nucleotides of the sequence was searched with BLAST2N in the sense strand with the following parameters (W 6, S 10, E 1000, and identity 90%). Finally, patented sequences and ORF homologies were searched using, respectively, BLASTN and BLASTP on GenSEQ
- 10 (Derwent's database of patented nucleotide sequences) and SWISSPROT for ORFs with the following parameters (W = 8 and B = 10). Before examining the extended full length cDNAs for sequences of interest, extended cDNAs which are not of interest are searched as follows.

#### a) Elimination of undesired sequences

Although 5'ESTs were checked to remove contaminant sequences as described in Example 18, a last verification was carried out to identify extended cDNAs sequences derived from undesired sequences such as vector RNAs, transfer RNAs, ribosomal rRNAs, mitochondrial RNAs, prokaryotic RNAs and fungal RNAs using the FASTA and BLASTN programs on both strands of extended cDNAs as described below.

To identify the extended cDNAs encoding vector RNAs, extended cDNAs are compared to the known sequences of vector RNA using the FASTA program. Sequences of extended cDNAs with more than 90% homology over stretches of 15 nucleotides are identified as vector RNA.

To identify the extended cDNAs encoding tRNAs, extended cDNA sequences were compared to the sequences of 1190 known tRNAs obtained from EMBL release 38, of which 100 were human. Sequences of extended cDNAs having more than 80% homology over 60 nucleotides using FASTA were identified as tRNA.

To identify the extended cDNAs encoding rRNAs, extended cDNA sequences were compared to the sequences of 2497 known rRNAs obtained from EMBL release 38, of which 73 were human. Sequences of extended cDNAs having more than 80% homology over stretches longer than 40 nucleotides using BLASTN were identified as rRNAs.

To identify the extended cDNAs encoding mtRNAs, extended cDNA sequences were compared to the sequences of the two known mitochondrial genomes for which the entire genomic sequences are available and all sequences transcribed from these mitochondrial genomes including tRNAs, rRNAs, and mRNAs for a total of 38 sequences. Sequences of extended cDNAs having more than 80% homology over stretches longer than 40 nucleotides using BLASTN were identified as mtRNAs.

Sequences which might have resulted from other exogenous contaminants were identified by comparing extended cDNA sequences to release 105 of Genbank bacterial and fungal divisions. Sequences of extended cDNAs

having more than 90% homology over 40 nucleotides using BLASTN were identified as exogenous prokaryotic or fungal contaminants.

In addition, extended cDNAs were searched for different repeat sequences, including Alu sequences, L1 sequences, THE and MER repeats, SSTR sequences or satellite, micro-satellite, or telomeric repeats. Sequences of extended cDNAs with more than 70% homology over 40 nucleotide stretches using BLASTN were identified as repeat sequences and masked in further identification procedures. In addition, clones showing extensive homology to repeats, i.e., matches of either more than 50 nucleotides if the homology was at least 75% or more than 40 nucleotides if the homology was at least 90%, were flagged.

#### b) Identification of structural features

10

20

25

Structural features, e.g. polyA tail and polyadenylation signal, of the sequences of full length extended cDNAs are subsequently determined as follows.

A polyA tail is defined as a homopolymeric stretch of at least 11 A with at most one alternative base within it.

The polyA tail search is restricted to the last 20 nt of the sequence and limited to stretches of 11 consecutive A's because sequencing reactions are often not readable after such a polyA stretch. Stretches with 100% homology over 6 nucleotides are identified as polyA tails.

To search for a polyadenylation signal, the polyA tail is clipped from the full-length sequence. The 50 bp preceding the polyA tail are searched for the canonic polyadenylation AAUAAA signal allowing one mismatch to account for possible sequencing errors and known variation in the canonical sequence of the polyadenylation signal.

#### c) Identification of functional features

Functional features, e.g. ORFs and signal sequences, of the sequences of full length extended cDNAs were subsequently determined as follows.

The 3 upper strand frames of extended cDNAs are searched for ORFs defined as the maximum length fragments beginning with a translation initiation codon and ending with a stop codon. ORFs encoding at least 20 amino acids are preferred.

Each found ORF is then scanned for the presence of a signal peptide in the first 50 amino-acids or, where appropriate, within shorter regions down to 20 amino acids or less in the ORF, using the matrix method of von Heijne (Nuc. Acids Res. 14: 4683-4690 (1986)) and the modification described in Example 22.

#### d) Homology to either nucleotidic or proteic sequences

Sequences of full length extended cDNAs are then compared to known sequences on a nucleotidic or proteic 30 basis.

Sequences of full length extended cDNAs are compared to the following known nucleic acid sequences: vertebrate sequences (Genbank), EST sequences (Genbank), patented sequences (Geneseqn) and recently identified sequences (Genbank daily releases) available at the time of filing for the priority documents. Full length cDNA sequences are also compared to the sequences of a private database (Genset internal sequences) in order to find sequences that

have already been identified by applicants. Sequences of full length extended cDNAs with more than 90% homology over 30 nucleotides using either BLASTN or BLAST2N as indicated in Table III are identified as sequences that have already been described. Matching vertebrate sequences are subsequently examined using FASTA; full length extended cDNAs with more than 70% homology over 30 nucleotides are identified as sequences that have already been described.

ORFs encoded by full length extended cDNAs as defined in section c) are subsequently compared to known amino acid sequences found in Swissprot release CHP, PIR release PIR# and Genpept release GPEPT public databases using BLASTP with the parameter W = 8 and allowing a maximum of 10 matches. Sequences of full length extended cDNAs showing extensive homology to known protein sequences are recognized as already identified proteins.

In addition, the three-frame conceptual translation products of the top strand of full length extended cDNAs

10 are compared to publicly known amino acid sequences of Swissprot using BLASTX with the parameter E = 0.001.

Sequences of full length extended cDNAs with more than 70% homology over 30 amino acid stretches are detected as already identified proteins.

#### Selection of Cloned Full Length Sequences of the Present Invention

Cloned full length extended cDNA sequences that have already been characterized by the aforementioned computer analysis are then submitted to an automatic procedure in order to preselect full length extended cDNAs containing sequences of interest.

#### a) Automatic sequence preselection

All complete cloned full length extended cDNAs clipped for vector on both ends are considered. First, a negative selection is operated in order to eliminate unwanted cloned sequences resulting from either contaminants or PCR artifacts as follows. Sequences matching contaminant sequences such as vector RNA, tRNA, mtRNA, rRNA sequences are discarded as well as those encoding ORF sequences exhibiting extensive homology to repeats as defined in section 4 a). Sequences obtained by direct cloning using nested primers on 5' and 3' tags (section 1. case a) but lacking polyA tail are discarded. Only ORFs containing a signal peptide and ending either before the polyA tail (case a) or before the end of the cloned 3'UTR (case b) are kept. Then, ORFs containing unlikely mature proteins such as mature proteins which size is less than 20 amino acids or less than 25% of the immature protein size are eliminated.

In the selection of the OFR, priority was given to the ORF and the frame corresponding to the polypeptides described in SignalTag Patents (United States Patent Application Serial Nos: 08/905,223; 08/905,135; 08/905,051; 08/905,144; 08/905,279; 08/904,468; 08/905,134; and 08/905,133). If the ORF was not found among the OFRs described in the SignalTag Patents, the ORF encoding the signal peptide with the highest score according to Von Heijne method as defined in Example 22 was chosen. If the scores were identical, then the longest ORF was chosen.

Sequences of full length extended cDNA clones are then compared pairwise with BLAST after masking of the repeat sequences. Sequences containing at least 90% homology over 30 nucleotides are clustered in the same class. Each cluster is then subjected to a cluster analysis that detects sequences resulting from internal priming or from

alternative splicing, identical sequences or sequences with several frameshifts. This automatic analysis serves as a basis for manual selection of the sequences.

#### b) Manual sequence selection

30

Manual selection is carried out using automatically generated reports for each sequenced full length extended cDNA clone. During this manual procedures, a selection is operated between clones belonging to the same class as follows. ORF sequences encoded by clones belonging to the same class are aligned and compared. If the homology between nucleotidic sequences of clones belonging to the same class is more than 90% over 30 nucleotide stretches or if the homology between amino acid sequences of clones belonging to the same class is more than 80% over 20 amino acid stretches, than the clones are considered as being identical. The chosen ORF is the best one according to the criteria mentioned below. If the nucleotide and amino acid homologies are less than 90% and 80% respectively, the clones are said to encode distinct proteins which can be both selected if they contain sequences of interest.

Selection of full length extended cDNA clones encoding sequences of interest is performed using the following criteria. Structural-parameters (initial tag, polyadenylation site and signal) are first checked. Then, homologies with known nucleic acids and proteins are examined in order to determine whether the clone sequence match a known nucleic/proteic sequence and, in the latter case, its covering rate and the date at which the sequence became public. If there is no extensive match with sequences other than ESTs or genomic DNA, or if the clone sequence brings substantial new information, such as encoding a protein resulting from alternative slicing of an mRNA coding for an already known protein, the sequence is kept. Examples of such cloned full length extended cDNAs containing sequences of interest are described in Example 28. Sequences resulting from chimera or double inserts as assessed by homology to other

#### **EXAMPLE 28**

#### Cloning and Sequencing of Extended cDNAs

The procedure described in Example 27 above was used to obtain the extended cDNAs of the present invention. Using this approach, the full length cDNA of SEQ ID NO:17 was obtained. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide MKKVLLLITAILAVAVG (SEQ ID NO: 18) having a von Heijne score of 8.2.

The full length cDNA of SEQ ID NO:19 was also obtained using this procedure. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide MWWFQQGLSFLPSALVIWTSA (SEQ ID NO:20) having a von Heijne score of 5.5.

Another full length cDNA obtained using the procedure described above has the sequence of SEQ ID NO:21.

This cDNA, falls into the "EST-ext" category described above and encodes the signal peptide

MVLTTLPSANSANSPVNMPTTGPNSLSYASSALSPCLT (SEQ ID NO:22) having a von Heijne score of 5.9.

40

The above procedure was also used to obtain a full length cDNA having the sequence of SEQ ID NO:23. This cDNA falls into the "EST-ext" category described above and encodes the signal peptide ILSTVTALTFAXA (SEQ ID NO:24) having a von Heijne score of 5.5.

The full length cDNA of SEQ ID NO:25 was also obtained using this procedure. This cDNA falls into the "new" category described above and encodes a signal peptide LVLTLCTLPLAVA (SEQ ID NO:26) having a von Heijne score of 10.1.

The full length cDNA of SEQ ID NO:27 was also obtained using this procedure. This cDNA falls into the "new" category described above and encodes a signal peptide LWLLFFLVTAIHA (SEQ ID NO:28) having a von Heijne score of 10.7.

The above procedures were also used to obtain the extended cDNAs of the present invention. 5' ESTs expressed in a variety of tissues were obtained as described above. The appended sequence listing provides the tissues from which the extended cDNAs were obtained. It will be appreciated that the extended cDNAs may also be expressed in tissues other than the tissue listed in the sequence listing.

5' ESTs obtained as described above were used to obtain extended cDNAs having the sequences of SEQ ID

NOs: 40-140 and 242-377. Table IV provides the sequence identification numbers of the extended cDNAs of the present invention, the locations of the full coding sequences in SEQ ID NOs: 40-140 and 242-377 (i.e. the nucleotides encoding both the signal peptide and the mature protein, listed under the heading FCS location in Table IV), the locations of the nucleotides in SEQ ID NOs: 40-140 and 242-377 which encode the signal peptides (listed under the heading SigPep Location in Table IV), the locations of the nucleotides in SEQ ID NOs: 40-140 and 242-377 which encode the mature proteins generated by cleavage of the signal peptides (listed under the heading Mature Polypeptide Location in Table IV), the locations in SEQ ID NOs: 40-140 and 242-377 of stop codons (listed under the heading Stop Codon Location in Table IV), the locations in SEQ ID NOs: 40-140 and 242-377 of polyA signals (listed under the heading Poly A Signal Location in Table IV) and the locations of polyA sites (listed under the heading Poly A Site Location in Table IV).

The polypeptides encoded by the extended cDNAs were screened for the presence of known structural or

25 functional motifs or for the presence of signatures, small amino acid sequences which are well conserved amongst the
members of a protein family. The conserved regions have been used to derive consensus patterns or matrices included in
the PROSITE data bank, in particular in the file prosite.dat (Release 13.0 of November 1995, located at
http://expasy.hcuge.ch/sprot/prosite.html. Prosite\_convert and prosite\_scan programs
(http://ulrec3.unil.ch/ftpserveur/prosite\_scan) were used to find signatures on the extended cDNAs.

For each pattern obtained with the prosite\_convert program from the prosite.dat file, the accuracy of the detection on a new protein sequence has been tested by evaluating the frequency of irrelevant hits on the population of human secreted proteins included in the data bank SWISSPROT. The ratio between the number of hits on shuffled proteins (with a window size of 20 amino acids) and the number of hits on native (unshuffled) proteins was used as an index. Every pattern for which the ration was greater than 20% (one hit on shuffled proteins for 5 hits on native

proteins) was skipped during the search with prosite\_scan. The program used to shuffle protein sequences (db\_shuffled) and the program used to determine the statistics for each pattern in the protein data banks (prosite\_statistics) are available on the ftp site http://ulrec3.unil.ch/ftpserveur/prosite\_scan.

Table V lists the sequence identification numbers of the polypeptides of SEQ ID NOs: 141-241 and 378-513, the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the full length polypeptide (second column), the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the signal peptides (third column), and the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the mature polypeptide created by cleaving the signal peptide from the full length polypeptide (fourth column).

The nucleotide sequences of the sequences of SEQ ID NOs: 40-140 and 242-377 and the amino acid sequences

10 encoded by SEQ ID NOs: 40-140 and 242-377 (i.e. amino acid sequences of SEQ ID NOs: 141-241 and 378-513) are

provided in the appended sequence listing. In some instances, the sequences are preliminary and may include some
incorrect or ambiguous sequences or amino acids. The sequences of SEQ ID NOs: 40-140 and 242-377 can readily be
screened for any errors therein and any sequence ambiguities can be resolved by resequencing a fragment containing
such errors or ambiguities on both strands. Nucleic acid fragments for resolving sequencing errors or ambiguities may be
obtained from the deposited clones or can be isolated using the techniques described herein. Resolution of any such
ambiguities or errors may be facilitated by using primers which hybridize to sequences located close to the ambiguous or
erroneous sequences. For example, the primers may hybridize to sequences within 50-75 bases of the ambiguity or
error. Upon resolution of an error or ambiguity, the corresponding corrections can be made in the protein sequences
encoded by the DNA containing the error or ambiguity. For example, in the sequences of the present invention, ambiguities
in the sequence of SEQ ID NO: 131 were resolved. The amino acid sequence of the protein encoded by a particular clone
can also be determined by expression of the clone in a suitable host cell, collecting the protein, and determining its
sequence.

For each amino acid sequence, Applicants have identified what they have determined to be the reading frame best identifiable with sequence information available at the time of filing. Some of the amino acid sequences may contain "Xaa" designators. These "Xaa" designators indicate either (1) a residue which cannot be identified because of nucleotide sequence ambiguity or (2) a stop codon in the determined sequence where Applicants believe one should not exist (if the sequence were determined more accurately).

Cells containing the extended cDNAs (SEQ ID NOs: 40-140 and 242-377) of the present invention in the vector pED6dpc2, are maintained in permanent deposit by the inventors at Genset, S.A., 24 Rue Royale, 75008 Paris, France.

Pools of cells containing the extended cDNAs (SEO ID NOs: 40-140 and 242-377), from which cells containing a particular polynucleotide are obtainable, were deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209 or the European Collection of Cell Cultures, Vaccine Research and Production Laboratory, Public Health Laboratory Service, Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire SP4 OJG, United Kingdom. Each extended cDNA clone has been transfected into separate bacterial cells (E-

coli) for this composite deposit. Table VI lists the deposit numbers of the clones containing the extended cDNAs of the present invention. Table VII provides the internal designation number assigned to each SEQ ID NO and indicates whether the sequence is a nucleic acid sequence or a protein sequence.

Each extended cDNA can be removed from the pED6dpc2 vector in which it was deposited by performing a

Notl, Pstl double digestion to produce the appropriate fragment for each clone. The proteins encoded by the extended cDNAs may also be expressed from the promoter in pED6dpc2.

Bacterial cells containing a particular clone can be obtained from the composite deposit as follows:

An oligonucleotide probe or probes should be designed to the sequence that is known for that particular clone.

This sequence can be derived from the sequences provided herein, or from a combination of those sequences. The design of the oligonucleotide probe should preferably follow these parameters:

- (a) It should be designed to an area of the sequence which has the fewest ambiguous bases ("N's"), if any;
- (b) Preferably, the probe is designed to have a  $T_m$  of approx. 80°C (assuming 2 degrees for each A or T and 4 degrees for each G or C). However, probes having melting temperatures between 40 °C and 80 °C may also be used provided that specificity is not lost.
- The oligonucleotide should preferably be labeled with (-[32P]ATP (specific activity 6000 Ci/mmole) and T4 polynucleotide kinase using commonly employed techniques for labeling oligonucleotides. Other labeling techniques can also be used. Unincorporated label should preferably be removed by gel filtration chromatography or other established methods. The amount of radioactivity incorporated into the probe should be quantified by measurement in a scintillation counter. Preferably, specific activity of the resulting probe should be approximately 4X10<sup>6</sup> dpm/pmole.
- The bacterial culture containing the pool of full-length clones should preferably be thawed and 100 µl of the stock used to inoculate a sterile culture flask containing 25 ml of sterile L-broth containing ampicillin at 100 µg/ml. The culture should preferably be grown to saturation at 37°C, and the saturated culture should preferably be diluted in fresh L-broth. Aliquots of these dilutions should preferably be plated to determine the dilution and volume which will yield approximately 5000 distinct and well-separated colonies on solid bacteriological media containing L-broth containing ampicillin at 100 µg/ml and agar at 1.5% in a 150 mm petri dish when grown overnight at 37°C. Other known methods of obtaining distinct, well-separated colonies can also be employed.

Standard colony hybridization procedures should then be used to transfer the colonies to nitrocellulose filters and lyse, denature and bake them.

The filter is then preferably incubated at 65°C for 1 hour with gentle agitation in 6X SSC (20X stock is 175.3 g NaC1/liter, 88.2 g Na citrate/liter, adjusted to pH 7.0 with NaOH) containing 0.5% SDS, 100 pg/ml of yeast RNA, and 10 mM EDTA (approximately 10 mL per 150 mm filter). Preferably, the probe is then added to the hybridization mix at a concentration greater than or equal to 1X10<sup>6</sup> dpm/mL. The filter is then preferably incubated at 65°C with gentle agitation overnight. The filter is then preferably washed in 500 mL of 2X SSC/0.1% SDS at room temperature with gentle shaking for 15 minutes. A third wash with 0.1X SSC/0.5% SDS at 65°C for 30 minutes to

WO 99/31236 PCT/IB98/02122

1 hour is optional. The filter is then preferably dried and subjected to autoradiography for sufficient time to visualize the positives on the X-ray film. Other known hybridization methods can also be employed.

The positive colonies are picked, grown in culture, and plasmid DNA isolated using standard procedures. The clones can then be verified by restriction analysis, hybridization analysis, or DNA sequencing.

The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the extended cDNA insertion. For example, a PCR reaction may be conducted using a primer having the sequence GGCCATACACTTGAGTGAC (SEQ ID NO:38) and a primer having the sequence ATATAGACAAACGCACACC (SEQ. ID. NO:39). The PCR product which corresponds to the extended cDNA can then be manipulated using standard cloning 10 techniques familiar to those skilled in the art.

In addition to PCR based methods for obtaining extended cDNAs, traditional hybridization based methods may also be employed. These methods may also be used to obtain the genomic DNAs which encode the mRNAs from which the 5' ESTs were derived, mRNAs corresponding to the extended cDNAs, or nucleic acids which are homologous to extended cDNAs or 5' ESTs. Example 29 below provides an example of such methods.

15

30

5

#### **EXAMPLE 29**

### Methods for Obtaining Extended cDNAs or Nucleic Acids Homologous to Extended cDNAs or 5' ESTs

A full length cDNA library can be made using the strategies described in Examples 13, 14, 15, and 16 above by replacing the random nonamer used in Example 14 with an oligo-dT primer. For instance, the oligonucleotide of SEQ ID 20 NO:14 may be used.

Alternatively, a cDNA library or genomic DNA library may be obtained from a commercial source or made using techniques familiar to those skilled in the art. The library includes cDNAs which are derived from the mRNA corresponding to a 5' EST or which have homology to an extended cDNA or 5' EST. The cDNA library or genomic DNA library is hybridized to a detectable probe comprising at least 10 consecutive nucleotides from the 5' EST or extended 25 cDNA using conventional techniques. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST or extended cDNA. More preferably, the probe comprises at least 20-30 consecutive nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises at least 30 nucleotides from the 5' EST or extended cDNA. In other embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the 5' EST or extended cDNA.

Techniques for identifying cDNA clones in a cDNA library which hybridize to a given probe sequence are disclosed in Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989. The same techniques may be used to isolate genomic DNAs.

Briefly, cDNA or genomic DNA clones which hybridize to the detectable probe are identified and isolated for further manipulation as follows. A probe comprising at least 10 consecutive nucleotides from the 5' EST or extended cDNA is labeled with a detectable label such as a radioisotope or a fluorescent molecule. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST or extended cDNA. More preferably, the probe comprises 20-30 consecutive nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises more than 30 nucleotides from the 5' EST or extended cDNA. In some embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the 5' EST or extended cDNA.

Techniques for labeling the probe are well known and include phosphorylation with polynucleotide kinase, nick translation, in vitro transcription, and non-radioactive techniques. The cDNAs or genomic DNAs in the library are transferred to a nitrocellulose or nylon filter and denatured. After incubation of the filter with a blocking solution, the filter is contacted with the labeled probe and incubated for a sufficient amount of time for the probe to hybridize to cDNAs or genomic DNAs containing a sequence capable of hybridizing to the probe.

By varying the stringency of the hybridization conditions used to identify extended cDNAs or genomic DNAs which hybridize to the detectable probe, extended cDNAS having different levels of homology to the probe can be identified and isolated. To identify extended cDNAs or genomic DNAs having a high degree of homology to the probe sequence, the melting temperature of the probe may be calculated using the following formulas:

For probes between 14 and 70 nucleotides in length the melting temperature (Tm) is calculated using the formula: Tm = 81.5 + 16.6(log [Na +]) + 0.41(fraction G + C)-(600/N) where N is the length of the probe.

If the hybridization is carried out in a solution containing formamide, the melting temperature may be calculated using the equation Tm = 81.5 + 16.6(log [Na +]) + 0.41(fraction G + C) + (0.63% formamide) + (600/N) where N is the length of the probe.

Prehybridization may be carried out in 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100µg denatured fragmented salmon sperm DNA or 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100µg denatured fragmented salmon sperm DNA, 50% formamide. The formulas for SSC and Denhardt's solutions are listed in Sambrook et al., supra.

Hybridization is conducted by adding the detectable probe to the prehybridization solutions listed above. Where
the probe comprises double stranded DNA, it is denatured before addition to the hybridization solution. The filter is
contacted with the hybridization solution for a sufficient period of time to allow the probe to hybridize to extended
cDNAs or genomic DNAs containing sequences complementary thereto or homologous thereto. For probes over 200
nucleotides in length, the hybridization may be carried out at 15-25°C below the Tm. For shorter probes, such as
oligonucleotide probes, the hybridization may be conducted at 15-25°C below the Tm. Preferably, for hybridizations in
6X SSC, the hybridization is conducted at approximately 68°C. Preferably, for hybridizations in 50% formamide
containing solutions, the hybridization is conducted at approximately 42°C.

All of the foregoing hybridizations would be considered to be under "stringent" conditions. Following hybridization, the filter is washed in 2X SSC, 0.1% SDS at room temperature for 15 minutes. The filter is then washed

PCT/IB98/02122

with 0.1X SSC, 0.5% SDS at room temperature for 30 minutes to 1 hour. Thereafter, the solution is washed at the hybridization temperature in 0.1X SSC, 0.5% SDS. A final wash is conducted in 0.1X SSC at room temperature.

Extended cDNAs, nucleic acids homologous to extended cDNAs or 5' ESTs, or genomic DNAs which have hybridized to the probe are identified by autoradiography or other conventional techniques.

The above procedure may be modified to identify extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs having decreasing levels of homology to the probe sequence. For example, to obtain extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs of decreasing homology to the detectable probe, less stringent conditions may be used. For example, the hybridization temperature may be decreased in increments of 5°C from 68°C to 42°C in a hybridization buffer having a Na+ concentration of approximately 1M. Following hybridization, the filter may be washed with 2X SSC, 0.5% SDS at the temperature of hybridization. These conditions are considered to be "moderate" conditions above 50°C and "low" conditions below 50°C.

Alternatively, the hybridization may be carried out in buffers, such as 6X SSC, containing formamide at a temperature of 42°C. In this case, the concentration of formamide in the hybridization buffer may be reduced in 5% increments from 50% to 0% to identify clones having decreasing levels of homology to the probe. Following hybridization, the filter may be washed with 6X SSC, 0.5% SDS at 50°C. These conditions are considered to be "moderate" conditions above 25% formamide and "low" conditions below 25% formamide.

Extended cDNAs, nucleic acids homologous to extended cDNAs, or genomic DNAs which have hybridized to the probe are identified by autoradiography.

If it is desired to obtain nucleic acids homologous to extended cDNAs, such as allelic variants thereof or nucleic acids encoding proteins related to the proteins encoded by the extended cDNAs, the level of homology between the hybridized nucleic acid and the extended cDNA or 5' EST used as the probe may readily be determined. To determine the level of homology between the hybridized nucleic acid and the extended cDNA or 5'EST from which the probe was derived, the nucleotide sequences of the hybridized nucleic acid and the extended cDNA or 5'EST from which the probe was derived are compared. For example, using the above methods, nucleic acids having at least 95% nucleic acid homology to the extended cDNA or 5'EST from which the probe was derived may be obtained and identified. Similarly, by using progressively less stringent hybridization conditions one can obtain and identify nucleic acids having at least 90%, at least 85%, at least 80% or at least 75% homology to the extended cDNA or 5'EST from which the probe was derived. The level of homology between the hybridized nucleic acid and the extended cDNA or 5'EST used as the probe may be further determined using BLAST2N; parameters may be adapted depending on the sequence length and degree of homology studied. In such comparisons, the default parameters or the parameters listed in Tables II and III may be used.

To determine whether a clone encodes a protein having a given amount of homology to the protein encoded by the extended cDNA or 5' EST, the amino acid sequence encoded by the extended cDNA or 5' EST is compared to the amino acid sequence encoded by the hybridizing nucleic acid. Homology is determined to exist when an amino acid sequence in the extended cDNA or 5' EST is closely related to an amino acid sequence in the hybridizing nucleic acid. A

 $u_{\mu_1}$ 

sequence is closely related when it is identical to that of the extended cDNA or 5' EST or when it contains one or more amino acid substitutions therein in which amino acids having similar characteristics have been substituted for one another. Using the above methods, one can obtain nucleic acids encoding proteins having at least 95%, at least 90%, at least 85%, at least 80% or at least 75% homology to the proteins encoded by the extended cDNA or 5'EST from which the probe was derived. Using the above methods and algorithms such as FASTA with parameters depending on the sequence length and degree of homology studied the level of homology may be determined. In determining the level of homology using FASTA, the default parameters or the parameters listed in Tables II or III may be used.

Alternatively, extended cDNAs may be prepared by obtaining mRNA from the tissue, cell, or organism of interest using mRNA preparation procedures utilizing poly A selection procedures or other techniques known to those skilled in the art. A first primer capable of hybridizing to the poly A tail of the mRNA is hybridized to the mRNA and a reverse transcription reaction is performed to generate a first cDNA strand.

The first cDNA strand is hybridized to a second primer containing at least 10 consecutive nucleotides of the sequences of the 5' EST for which an extended cDNA is desired. Preferably, the primer comprises at least 12, 15, or 17 consecutive nucleotides from the sequences of the 5' EST. More preferably, the primer comprises 20-30 consecutive nucleotides from the sequences of the 5' EST. In some embodiments, the primer comprises more than 30 nucleotides from the sequences of the 5' EST. If it is desired to obtain extended cDNAs containing the full protein coding sequence, including the authentic translation initiation site, the second primer used contains sequences located upstream of the translation initiation site. The second primer is extended to generate a second cDNA strand complementary to the first cDNA strand. Alternatively, RTPCR may be performed as described above using primers from both ends of the cDNA to be obtained.

Extended cDNAs containing 5' fragments of the mRNA may be prepared by contacting an mRNA comprising the sequence of the 5' EST for which an extended cDNA is desired with a primer comprising at least 10 consecutive nucleotides of the sequences complementary to the 5' EST, hybridizing the primer to the mRNAs, and reverse transcribing the hybridized primer to make a first cDNA strand from the mRNAs. Preferably, the primer comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST. More preferably, the primer comprises 20-30 consecutive nucleotides from the 5' EST.

Thereafter, a second cDNA strand complementary to the first cDNA strand is synthesized. The second cDNA strand may be made by hybridizing a primer complementary to sequences in the first cDNA strand to the first cDNA strand and extending the primer to generate the second cDNA strand.

The double stranded extended cDNAs made using the methods described above are isolated and cloned. The extended cDNAs may be cloned into vectors such as plasmids or viral vectors capable of replicating in an appropriate host cell. For example, the host cell may be a bacterial, mammalian, avian, or insect cell.

Techniques for isolating mRNA, reverse transcribing a primer hybridized to mRNA to generate a first cDNA strand, extending a primer to make a second cDNA strand complementary to the first cDNA strand, isolating the double

stranded cDNA and cloning the double stranded cDNA are well known to those skilled in the art and are described in Current Protocols in Molecular Biology, John Wiley 503 Sons, Inc. 1997 and Sambrook et al. Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989.

Alternatively, kits for obtaining full length cDNAs, such as the GeneTrapper (Cat. No. 10356-020, Gibco, BRL),

may be used for obtaining full length cDNAs or extended cDNAs. In this approach, full length or extended cDNAs are
prepared from mRNA and cloned into double stranded phagemids. The cDNA library in the double stranded phagemids is
then rendered single stranded by treatment with an endonuclease, such as the Gene II product of the phage F1, and
Exonuclease III as described in the manual accompanying the GeneTrapper kit. A biotinylated oligonucleotide comprising
the sequence of a 5' EST, or a fragment containing at least 10 nucleotides thereof, is hybridized to the single stranded
phagemids. Preferably, the fragment comprises at least 12, 15, or 17 consecutive nucleotides from the 5' EST. More
preferably, the fragment comprises 20-30 consecutive nucleotides from the 5' EST. In some procedures, the fragment
may comprise more than 30 consecutive nucleotides from the 5' EST. For example, the fragment may comprises at least
40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the 5' EST.

Hybrids between the biotinylated oligonucleotide and phagemids having inserts containing the 5' EST sequence are isolated by incubating the hybrids with streptavidin coated paramagnetic beads and retrieving the beads with a magnet. Thereafter, the resulting phagemids containing the 5' EST sequence are released from the beads and converted into double stranded DNA using a primer specific for the 5' EST sequence. The resulting double stranded DNA is transformed into bacteria. Extended cDNAs containing the 5' EST sequence are identified by colony PCR or colony hybridization.

A plurality of extended cDNAs containing full length protein coding sequences or sequences encoding only the mature protein remaining after the signal peptide is cleaved may be provided as cDNA libraries for subsequent evaluation of the encoded proteins or use in diagnostic assays as described below.

#### IV. Expression of Proteins Encoded by Extended cDNAs Isolated Using 5' ESTs

Extended cDNAs containing the full protein coding sequences of their corresponding mRNAs or portions

thereof, such as cDNAs encoding the mature protein, may be used to express the secreted proteins or portions thereof which they encode as described in Example 30 below. If desired, the extended cDNAs may contain the sequences encoding the signal peptide to facilitate secretion of the expressed protein. It will be appreciated that a plurality of extended cDNAs containing the full protein coding sequences or portions thereof may be simultaneously cloned into expression vectors to create an expression library for analysis of the encoded proteins as described below.

30 EXAMPLE 30

#### Expression of the Proteins Encoded by Extended cDNAs or Portions Thereof

To express the proteins encoded by the extended cDNAs or portions thereof, nucleic acids containing the coding sequence for the proteins or portions thereof to be expressed are obtained as described in Examples 27-29 and cloned into a suitable expression vector. If desired, the nucleic acids may contain the sequences encoding the signal

peptide to facilitate secretion of the expressed protein. For example, the nucleic acid may comprise the sequence of one of SEO ID NOs: 40-140 and 242-377 listed in Table IV and in the accompanying sequence listing. Alternatively, the nucleic acid may comprise those nucleotides which make up the full coding sequence of one of the sequences of SEQ ID NOs: 40-140 and 242-377 as defined in Table IV above.

5 It will be appreciated that should the extent of the full coding sequence (i.e. the sequence encoding the signal peptide and the mature protein resulting from cleavage of the signal peptide) differ from that listed in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, post-translational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the extent of the full coding sequences in the sequences of SEO ID NOs. 40-140 and 242-377. 10 For example, the sequence of SEO ID NO: 115 represents an alternatively spliced transcript of a previously identified mRNA.. Accordingly, the scope of any claims herein relating to nucleic acids containing the full coding sequence of one of SEQ ID NOs. 40-140 and 242-377 is not to be construed as excluding any readily identifiable variations from or equivalents to the full coding sequences listed in Table IV Similarly, should the extent of the full length polypeptides differ from those indicated in Table V as a result of any of the preceding factors, the scope of claims relating to polypeptides 15 comprising the amino acid sequence of the full length polypeptides is not to be construed as excluding any readily identifiable variations from or equivalents to the sequences listed in Table V.

Alternatively, the nucleic acid used to express the protein or portion thereof may comprise those nucleotides which encode the mature protein (i.e. the protein created by cleaving the signal peptide off) encoded by one of the sequences of SEO ID NOs: 40-140 and 242-377 as defined in Table IV above.

It will be appreciated that should the extent of the sequence encoding the mature protein differ from that listed in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, posttranslational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the extent of the sequence encoding the mature protein in the sequences of SEQ ID NOs. 40-140 and 242-377. Accordingly, the scope of any claims herein relating to nucleic acids 25 containing the sequence encoding the mature protein encoded by one of SEQ ID Nos. 40-140 and 242-377 is not to be construed as excluding any readily identifiable variations from or equivalents to the sequences listed in Table IV. Thus, claims relating to nucleic acids containing the sequence encoding the mature protein encompass equivalents to the sequences listed in Table IV, such as sequences encoding biologically active proteins resulting from post-translational modification, enzymatic cleavage, or other readily identifiable variations from or equivalents to the secreted proteins in 30 addition to cleavage of the signal peptide. Similarly, should the extent of the mature polypeptides differ from those indicated in Table V as a result of any of the preceding factors, the scope of claims relating to polypeptides comprising the sequence of a mature protein included in the sequence of one of SEQ ID NOs. 141-241 and 378-513 is not to be construed as excluding any readily identifiable variations from or equivalents to the sequences listed in Table V. Thus, claims relating to polypeptides comprising the sequence of the mature protein encompass equivalents to the sequences

listed in Table IV, such as biologically active proteins resulting from post-translational modification, enzymatic cleavage, or other readily identifiable variations from or equivalents to the secreted proteins in addition to cleavage of the signal peptide. It will also be appreciated that should the biologically active form of the polypeptides included in the sequence of one of SEQ ID NOs. 141-241 and 378-513 or the nucleic acids encoding the biologically active form of the polypeptides differ from those identified as the mature polypeptide in Table V or the nucleotides encoding the mature polypeptide in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, post-translational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the amino acids in the biologically active form of the polypeptides and the nucleic acids encoding the biologically active form of the polypeptides. In such instances, the claims relating to polypetides comprising the mature protein included in one of SEQ ID NOs. 141-241 and 378-513 or nucleic acids comprising the nucleotides of one of SEQ ID NOs. 40-140 and 242-377 encoding the mature protein shall not be construed to exclude any readily identifiable variations from the sequences listed in Table IV and Table V.

In some embodiments, the nucleic acid used to express the protein or portion thereof may comprise those nucleotides which encode the signal peptide encoded by one of the sequences of SEQ ID NOs: 40-140 and 242-377 as defined in Table IV above.

It will be appreciated that should the extent of the sequence encoding the signal peptide differ from that listed in Table IV as a result of a sequencing error, reverse transcription or amplification error, mRNA splicing, post-translational modification of the encoded protein, enzymatic cleavage of the encoded protein, or other biological factors, one skilled in the art would be readily able to identify the extent of the sequence encoding the signal peptide in the sequences of SEO ID Nos. 40-140 and 242-377. Accordingly, the scope of any claims herein relating to nucleic acids containing the sequence encoding the signal peptide encoded by one of SEO ID Nos. 40-140 and 242-377 is not to be construed as excluding any readily identifiable variations from the sequences listed in Table IV. Similarly, should the extent of the signal peptides differ from those indicated in Table V as a result of any of the preceding factors, the scope of claims relating to polypeptides comprising the sequence of a signal peptide included in the sequence of one of SEO ID Nos. 141-241 and 378-513 is not to be construed as excluding any readily identifiable variations from the sequences listed in Table V.

Alternatively, the nucleic acid may encode a polypeptide comprising at least 10 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In some embodiments, the nucleic acid may encode a polypeptide comprising at least 15 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In other embodiments, the nucleic acid may encode a polypeptide comprising at least 25 consecutive amino acids of one of the sequences of SEQ ID NOs: 141-241 and 378-513. In other embodiments, the nucleic acid may encode a polypeptide comprising at least 60, at least 75, at least 100 or more than 100 consecutive amino acids of one of the sequences of SEQ ID Nos: 141-241 and 378-513.

The nucleic acids inserted into the expression vectors may also contain sequences upstream of the sequences encoding the signal peptide, such as sequences which regulate expression levels or sequences which confer tissue specific expression.

The nucleic acid encoding the protein or polypeptide to be expressed is operably linked to a promoter in an expression vector using conventional cloning technology. The expression vector may be any of the mammalian, yeast, insect or bacterial expression systems known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Genetics Institute (Cambridge, MA), Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon context and codon pairing of the sequence may be optimized for the particular expression organism in which the expression vector is introduced, as explained by Hatfield, et al., U.S. Patent No. 5,082,767.

The following is provided as one exemplary method to express the proteins encoded by the extended cDNAs corresponding to the 5' ESTs or the nucleic acids described above. First, the methionine initiation codon for the gene and the poly A signal of the gene are identified. If the nucleic acid encoding the polypeptide to be expressed lacks a methionine to serve as the initiation site, an initiating methionine can be introduced next to the first codon of the nucleic acid using conventional techniques. Similarly, if the extended cDNA lacks a poly A signal, this sequence can be added to the construct by, for example, splicing out the Poly A signal from pSG5 (Stratagene) using Bgll and Sall restriction endonuclease enzymes and incorporating it into the mammalian expression vector pXT1 (Stratagene). pXT1 contains the LTRs and a portion of the gag gene from Moloney Murine Leukemia Virus. The position of the LTRs in the construct allow efficient stable transfection. The vector includes the Herpes Simplex Thymidine Kinase promoter and the selectable neomycin gene. The extended cDNA or portion thereof encoding the polypeptide to be expressed is obtained by PCR from the bacterial vector using oligonucleotide primers complementary to the extended cDNA or portion thereof and containing restriction endonuclease sequences for Pst I incorporated into the 5'primer and Bglll at the 5' end of the corresponding cDNA 3' primer, taking care to ensure that the extended cDNA is positioned in frame with the poly A signal. The purified fragment obtained from the resulting PCR reaction is digested with Pstl, blunt ended with an exonuclease, digested with Bglll, purified and ligated to pXT1, now containing a poly A signal and digested with Bglll.

The ligated product is transfected into mouse NIH 3T3 cells using Lipofectin (Life Technologies, Inc., Grand Island, New York) under conditions outlined in the product specification. Positive transfectants are selected after growing the transfected cells in 600ug/ml G418 (Sigma, St. Louis, Missouri). Preferably the expressed protein is released into the culture medium, thereby facilitating purification.

Alternatively, the extended cDNAs may be cloned into pED6dpc2 as described above. The resulting pED6dpc2 constructs may be transfected into a suitable host cell, such as COS 1 cells. Methotrexate resistant cells are selected and expanded. Preferably, the protein expressed from the extended cDNA is released into the culture medium thereby facilitating purification.

Proteins in the culture medium are separated by gel electrophoresis. If desired, the proteins may be ammonium sulfate precipitated or separated based on size or charge prior to electrophoresis.

As a control, the expression vector lacking a cDNA insert is introduced into host cells or organisms and the proteins in the medium are harvested. The secreted proteins present in the medium are detected using techniques such as Coomassie or silver staining or using antibodies against the protein encoded by the extended cDNA. Coomassie and silver staining techniques are familiar to those skilled in the art.

Antibodies capable of specifically recognizing the protein of interest may be generated using synthetic 15-mer peptides having a sequence encoded by the appropriate 5' EST, extended cDNA, or portion thereof. The synthetic peptides are injected into mice to generate antibody to the polypeptide encoded by the 5' EST, extended cDNA, or portion thereof.

Secreted proteins from the host cells or organisms containing an expression vector which contains the extended cDNA derived from a 5' EST or a portion thereof are compared to those from the control cells or organism. The presence of a band in the medium from the cells containing the expression vector which is absent in the medium from the control cells indicates that the extended cDNA encodes a secreted protein. Generally, the band corresponding to the protein encoded by the extended cDNA will have a mobility near that expected based on the number of amino acids in the open reading frame of the extended cDNA. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

Alternatively, if the protein expressed from the above expression vectors does not contain sequences directing its secretion, the proteins expressed from host cells containing an expression vector containing an insert encoding a secreted protein or portion thereof can be compared to the proteins expressed in host cells containing the expression vector without an insert. The presence of a band in samples from cells containing the expression vector with an insert which is absent in samples from cells containing the expression vector without an insert indicates that the desired protein or portion thereof is being expressed. Generally, the band will have the mobility expected for the secreted protein or portion thereof. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

The protein encoded by the extended cDNA may be purified using standard immunochromatography techniques.

In such procedures, a solution containing the secreted protein, such as the culture medium or a cell extract, is applied to a column having antibodies against the secreted protein attached to the chromatography matrix. The secreted protein is allowed to bind the immunochromatography column. Thereafter, the column is washed to remove non-specifically bound proteins. The specifically bound secreted protein is then released from the column and recovered using standard techniques.

If antibody production is not possible, the extended cDNA sequence or portion thereof may be incorporated into expression vectors designed for use in purification schemes employing chimeric polypeptides. In such strategies the coding sequence of the extended cDNA or portion thereof is inserted in frame with the gene encoding the other half of

the chimera. The other half of the chimera may be β-globin or a nickel binding polypeptide encoding sequence. A chromatography matrix having antibody to β-globin or nickel attached thereto is then used to purify the chimeric protein. Protease cleavage sites may be engineered between the β-globin gene or the nickel binding polypeptide and the extended cDNA or portion thereof. Thus, the two polypeptides of the chimera may be separated from one another by protease digestion.

One useful expression vector for generating β-globin chimerics is pSG5 (Stratagene), which encodes rabbit β-globin. Intron II of the rabbit β-globin gene facilitates splicing of the expressed transcript, and the polyadenylation signal incorporated into the construct increases the level of expression. These techniques as described are well known to those skilled in the art of molecular biology. Standard methods are published in methods texts such as Davis et al.,

(Basic Methods in Molecular Biology, L.G. Davis, M.D. Dibner, and J.F. Battey, ed., Elsevier Press, NY, 1986) and many of the methods are available from Stratagene, Life Technologies, Inc., or Promega. Polypeptide may additionally be produced from the construct using in vitro translation systems such as the In vitro Express<sup>TM</sup> Translation Kit (Stratagene).

Following expression and purification of the secreted proteins encoded by the 5' ESTs, extended cDNAs, or fragments thereof, the purified proteins may be tested for the ability to bind to the surface of various cell types as described in Example 31 below. It will be appreciated that a plurality of proteins expressed from these cDNAs may be included in a panel of proteins to be simultaneously evaluated for the activities specifically described below, as well as other biological roles for which assays for determining activity are available.

#### **EXAMPLE 31**

## 20 Analysis of Secreted Proteins to Determine Whether they Bind to the Cell Surface

The proteins encoded by the 5' ESTs, extended cDNAs, or fragments thereof are cloned into expression vectors such as those described in Example 30. The proteins are purified by size, charge, immunochromatography or other techniques familiar to those skilled in the art. Following purification, the proteins are labeled using techniques known to those skilled in the art. The labeled proteins are incubated with cells or cell lines derived from a variety of organs or tissues to allow the proteins to bind to any receptor present on the cell surface. Following the incubation, the cells are washed to remove non-specifically bound protein. The labeled proteins are detected by autoradiography. Alternatively, unlabeled proteins may be incubated with the cells and detected with antibodies having a detectable label, such as a fluorescent molecule, attached thereto.

Specificity of cell surface binding may be analyzed by conducting a competition analysis in which various amounts of unlabeled protein are incubated along with the labeled protein. The amount of labeled protein bound to the cell surface decreases as the amount of competitive unlabeled protein increases. As a control, various amounts of an unlabeled protein unrelated to the labeled protein is included in some binding reactions. The amount of labeled protein bound to the cell surface does not decrease in binding reactions containing increasing amounts of unrelated unlabeled protein, indicating that the protein encoded by the cDNA binds specifically to the cell surface.

As discussed above, secreted proteins have been shown to have a number of important physiological effects and, consequently, represent a valuable therapeutic resource. The secreted proteins encoded by the extended cDNAs or portions thereof made according to Examples 27-29 may be evaluated to determine their physiological activities as described below.

#### 5 EXAMPLE 32

. ', :

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Cytokine, Cell Proliferation or Cell Differentiation Activity

As discussed above, secreted proteins may act as cytokines or may affect cellular proliferation or differentiation. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B5, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7c and CMK. The proteins encoded by the above extended cDNAs or portions thereof may be evaluated for their ability to regulate T cell or thymocyte proliferation in assays such as those described above or in the following references: Current Protocols in Immunology, Ed. by J.E. Coligan et al., Greene Publishing Associates and Wiley-Interscience; Takai et al. J. Immunol. 137:3494-3500, 1986. Bertagnolli et al. J. Immunol. 145:1706-1712, 1990. Bertagnolli et al., Cellular Immunology 133:327-341, 1991. Bertagnolli, et al. J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152:1756-1761, 1994.

In addition, numerous assays for cytokine production and/or the proliferation of spleen cells, lymph node cells
and thymocytes are known. These include the techniques disclosed in Current Protocols in Immunology. J.E. Coligan
et al. Eds., Vol 1 pp. 3.12.1-3.12.14 John Wiley and Sons, Toronto. 1994; and Schreiber, R.D. Current Protocols in
Immunology., supra Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

The proteins encoded by the cDNAs may also be assayed for the ability to regulate the proliferation and differentiation of hematopoietic or lymphopoietic cells. Many assays for such activity are familiar to those skilled in the art, including the assays in the following references: Bottomly, K., Davis, L.S. and Lipsky, P.E., Measurement of Human and Murine Interleukin 2 and Interleukin 4, Current Protocols in Immunology., J.E. Coligan et al. Eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 36:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Nordan, R., Measurement of Mouse and Human Interleukin 6 Current Protocols in Immunology. J.E. Coligan et al. Eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Bennett, F., Giannotti, J., Clark, S.C. and Turner, K.J., Measurement of Human Interleukin 11 Current Protocols in Immunology. J.E. Coligan et al. Eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J., Measurement of Mouse and Human Interleukin 9 Current Protocols in Immunology. J.E. Coligan et al., Eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

The proteins encoded by the cDNAs may also be assayed for their ability to regulate T-cell responses to antigens. Many assays for such activity are familiar to those skilled in the art, including the assays described in the following references: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function), Chapter 6 (Cytokines and Their Cellular Receptors) and Chapter 7, (Immunologic Studies in Humans) in Current Protocols in Immunology, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Interscience; Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Those proteins which exhibit cytokine, cell proliferation, or cell differentiation activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which induction of cell proliferation or differentiation is beneficial. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 33**

### Assaying the Proteins Expressed from Extended cDNAs or Portions

#### Thereof for Activity as Immune System Regulators

The proteins encoded by the cDNAs may also be evaluated for their effects as immune regulators. For example, the proteins may be evaluated for their activity to influence thymocyte or splenocyte cytotoxicity. Numerous assays for such activity are familiar to those skilled in the art including the assays described in the following references: Chapter 3 (In Vitro Assays for Mouse Lymphocyte Function 3.1-3.19) and Chapter 7 (Immunologic studies in Humans) in Current Protocols in Immunology, J.E. Coligan et al. Eds, Greene Publishing Associates and Wiley-Interscience; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

The proteins encoded by the cDNAs may also be evaluated for their effects on T-cell dependent immunoglobulin responses and isotype switching. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Maliszewski, J. Immunol. 144:3028-3033, 1990; Mond, J.J. and Brunswick, M Assays for B Cell Function: *In vitro* Antibody Production, Vol 1 pp. 3.8.1-3.8.16 in Current Protocols in Immunology. J.E. Coligan et al Eds., John Wiley and Sons, Toronto. 1994.

The proteins encoded by the cDNAs may also be evaluated for their effect on immune effector cells, including their effect on Th1 cells and cytotoxic lymphocytes. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Chapter 3 (In Vitro Assays for Mouse Lymphocyte

Function 3.1-3.19) and Chapter 7 (Immunologic Studies in Humans) in Current Protocols in Immunology, J.E. Coligan et al. Eds., Greene Publishing Associates and Wiley-Interscience; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al.; J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

The proteins encoded by the cDNAs may also be evaluated for their effect on dendritic cell mediated activation
of naive T-cells. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264,
10 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

The proteins ercoded by the cDNAs may also be evaluated for their influence on the lifetime of lymphocytes.

Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Those proteins which exhibit activity as immune system regulators activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of immune activity is beneficial. For example, the protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis,

myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to regulate immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T-cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. 10 Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte 15 antigen functions (such as, for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 20 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an 25 immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed 30 using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4lg fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models

of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which 5 promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead 10 to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/pr/pr mice or NZB hybrid mice, murine autoimmuno collagen arthritis, diabetes mellitus in OD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory 20 form of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to T cells 25 in vivo, thereby activating the T cells.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be 30 transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acids encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and β<sub>2</sub> macroglobulin protein or an MHC class II α chain protein and an MHC class II β chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class II or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 34**

# Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Hematopoiesis Regulating Activity

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their hematopoiesis regulating activity. For example, the effect of the proteins on embryonic stem cell differentiation may be evaluated. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their influence on the lifetime of stem cells and stem cell differentiation. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Freshney, M.G. Methylcellulose Colony Forming Assays, in Culture of Hematopoietic Cells. R.I. Freshney, et al. Eds. pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; McNiece, I.K. and Briddell, R.A. Primitive Hematopoietic Colony Forming Cells with High Proliferative Potential, in Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Ploemacher, R.E. Cobblestone Area Forming Cell Assay, In Culture of Hematopoietic Cells. R.I. Freshney, et al. Eds. pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Spooncer, E., Dexter, M. and Allen, T. Long Term Bone Marrow Cultures in the Presence of Stromal Cells, in Culture of Hematopoietic Cells. R.I. Freshney, et al. Eds.

pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; and Sutherland, H.J. Long Term Culture Initiating Cell Assay, in Culture of Hematopoietic Cells. R.I. Freshney, et al. Eds. pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Those proteins which exhibit hematopoiesis regulatory activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of hematopoeisis is beneficial. For example, a protein of the present 5 invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid 10 cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelosuppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantion, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or 20 genetically manipulated for gene therapy. Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 35**

Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Tissue Growth

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their effect on tissue growth. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in International Patent Publication No. W095/16035, International Patent Publication No. W095/05846 and International Patent Publication No. W091/07491.

Assays for wound healing activity include, without limitation, those described in: Winter, <u>Epidermal Wound</u>

30 <u>Healing</u>, pps. 71-112 (Maibach, H1 and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Those proteins which are involved in the regulation of tissue growth may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of tissue growth is beneficial. For example, a protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or

nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and 5 other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to 20 tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate 25 growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of 30 nerve and brain tissue, i.e., for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium) muscle

(smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to generate. A protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokinc damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

20

15

5

#### **EXAMPLE 36**

# Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Reproductive Hormones or Cell Movement

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their ability to regulate reproductive hormones, such as follicle stimulating hormone. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986. Chapter 6.12 (Measurement of Alpha and Beta Chemokines) Current Protocols in Immunology, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Intersciece; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al. Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153:1762-1768, 1994.

Those proteins which exhibit activity as reproductive hormones or regulators of cell movement may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of reproductive hormones or cell movement are beneficial. For example, a protein of the present invention may also exhibit activin- or inhibin-related

الإرا

activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins are characterized by their ability to stimulate the release of folic stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin α family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals.

Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin-B group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 36A**

15

25

## Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Chemotactic/Chemokinetic Activity

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for chemotactic/chemokinetic activity. For example, a protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, cosinophils, epithelial and/or endothelial cells. Chemotactic and chmokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhension of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12,

Measurement of alpha and beta Chemokincs 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Mueller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol, 153:1762-1768, 1994.

#### **EXAMPLE 37**

5

# Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Regulation of Blood Clotting

The proteins encoded by the extended cDNAs or portions thereof may also be evaluated for their effects on blood clotting. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res.

10 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

Those proteins which are involved in the regulation of blood clotting may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of blood clotting is beneficial. For example, a protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulations disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke). Alternatively, as described in more detail below, genes encoding these proteins or nucleic acids regulating the expression of these proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

#### **EXAMPLE 38**

# Assaying the Proteins Expressed from Extended cDNAs or Portions Thereof for Involvement in Receptor/Ligand Interactions

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for their involvement in receptor/ligand interactions. Numerous assays for such involvement are familiar to those skilled in the art, including the assays disclosed in the following references: Chapter 7.28 (Measurement of Cellular Adhesion under Static Conditions 7.28.1-7.28.22) in Current Protocols in Immunology, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Interscience; Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160, 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995; Gyuris et al., Cell 75:791-803, 1993.

For example, the proteins of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion

molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune respones). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

#### **EXAMPLE 38A**

### Assaying the Proteins Expressed from Extended cDNAs or Portions

### Thereof for Anti-Inflammatory Activity

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusioninury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

#### 20

30

#### **EXAMPLE 38B**

# Assaying the Proteins Expressed from Extended cDNAs or

# Portions Thereof for Tumor Inhibition Activity

The proteins encoded by the extended cDNAs or a portion thereof may also be evaluated for tumor inhibition activity. In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, climinating or inhibiting factors, agents or cell types which promote tumor growth.

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or

WO 99/31236 Po

-64-

circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or climination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

#### **EXAMPLE 39**

# Identification of Proteins which Interact with Polypeptides Encoded by Extended cDNAs

Proteins which interact with the polypeptides encoded by extended cDNAs or portions thereof, such as

receptor proteins, may be identified using two hybrid systems such as the Matchmaker Two Hybrid System 2 (Catalog No. K1604-1, Clontech). As described in the manual accompanying the Matchmaker Two Hybrid System 2 (Catalog No. K1604-1, Clontech), the extended cDNAs or portions thereof, are inserted into an expression vector such that they are in frame with DNA encoding the DNA binding domain of the yeast transcriptional activator GAL4. cDNAs in a cDNA library which encode proteins which might interact with the polypeptides encoded by the extended cDNAs or portions thereof are inserted into a second expression vector such that they are in frame with DNA encoding the activation domain of GAL4. The two expression plasmids are transformed into yeast and the yeast are plated on selection medium which selects for expression of selectable markers on each of the expression vectors as well as GAL4 dependent expression of the HIS3 gene. Transformants capable of growing on medium lacking histidine are screened for GAL4 dependent lacZ expression. Those cells which are positive in both the histidine selection and the lacZ assay contain plasmids encoding proteins which interact with the polypeptide encoded by the extended cDNAs or portions thereof.

Alternatively, the system described in Lustig et al., Methods in Enzymology 283: 83-99 (1997) may be used for identifying molecules which interact with the polypeptides encoded by extended cDNAs. In such systems, *in vitro* transcription reactions are performed on a pool of vectors containing extended cDNA inserts cloned downstream of a promoter which drives *in vitro* transcription. The resulting pools of mRNAs are introduced into *Xenopus laevis* oocytes.

30 The oocytes are then assayed for a desired activity.

Alternatively, the pooled *in vitro* transcription products produced as described above may be translated *in vitro*. The pooled *in vitro* translation products can be assayed for a desired activity or for interaction with a known polypeptide.

Proteins or other molecules interacting with polypeptides encoded by extended cDNAs can be found by a variety of additional techniques. In one method, affinity columns containing the polypeptide encoded by the extended cDNA or a portion thereof can be constructed. In some versions, of this method the affinity column contains chimeric proteins in which the protein encoded by the extended cDNA or a portion thereof is fused to glutathione S-transferase. A mixture of cellular proteins or pool of expressed proteins as described above and is applied to the affinity column. Proteins interacting with the polypeptide attached to the column can then be isolated and analyzed on 2-D electrophoresis gel as described in Ramunsen et al. Electrophoresis, 18, 588-598 (1997). Alternatively, the proteins retained on the affinity column can be purified by electrophoresis based methods and sequenced. The same method can be used to isolate antibodies, to screen phage display products, or to screen phage display human antibodies.

Proteins interacting with polypeptides encoded by extended cDNAs or portions thereof can also be screened by using an Optical Biosensor as described in Edwards & Leatherbarrow, Analytical Biochemistry, 246, 1-6 (1997). The main advantage of the method is that it allows the determination of the association rate between the protein and other interacting molecules. Thus, it is possible to specifically select interacting molecules with a high or low association rate. Typically a target molecule is linked to the sensor surface (through a carboxymethl dextran matrix) and a sample of test molecules is placed in contact with the target molecules. The binding of a test molecule to the target molecule causes a change in the refractive index and/ or thickness. This change is detected by the Biosensor provided it occurs in the evanescent field (which extend a few hundred manometers from the sensor surface). In these screening assays, the target molecule can be one of the polypeptides encoded by extended cDNAs or a portion thereof and the test sample can be a collection of proteins extracted from tissues or cells, a pool of expressed proteins, combinatorial peptide and/ or 20 chemical libraries, or phage displayed peptides. The tissues or cells from which the test proteins are extracted can originate from any species.

In other methods, a target protein is immobilized and the test population is a collection of unique polypeptides encoded by the extended cDNAs or portions thereof.

To study the interaction of the proteins encoded by the extended cDNAs or portions thereof with drugs, the 25 microdialysis coupled to HPLC method described by Wang et al., Chromatographia, 44, 205-208(1997) or the affinity capillary electrophoresis method described by Busch et al., J. Chromatogr. 777:311-328 (1997), the disclosures of which are incorporated herein by referenc can be used.

The system described in U.S. Patent No. 5,654,150 may also be used to identify molecules which interact with the polypeptides encoded by the extended cDNAs. In this system, pools of extended cDNAs are transcribed and 30 translated in vitro and the reaction products are assayed for interaction with a known polypeptide or antibody.

It will be appreciated by those skilled in the art that the proteins expressed from the extended cDNAs or portions may be assayed for numerous activities in addition to those specifically enumerated above. For example, the expressed proteins may be evaluated for applications involving control and regulation of inflammation, tumor

proliferation or metastasis, infection, or other clinical conditions. In addition, the proteins expressed from the extended cDNAs or portions thereof may be useful as nutritional agents or cosmetic agents.

The proteins expressed from the extended cDNAs or portions thereof may be used to generate antibodies capable of specifically binding to the expressed protein or fragments thereof as described in Example 40 below. The antibodies may capable of binding a full length protein encoded by one of the sequences of SEQ ID NOs. 40-140 and 242-377, or a signal peptide encoded by one of the sequences of SEQ ID Nos. 40-140 and 242-377. Alternatively, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 10 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513. In some embodiments, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 15 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513. In other embodiments, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 25 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513. In further embodiments, the antibodies may be capable of binding fragments of the proteins expressed from the extended cDNAs which comprise at least 40 amino acids of the sequences of SEQ ID NOs: 141-241 and 378-513.

#### **EXAMPLE 40**

#### Production of an Antibody to a Human Protein

Substantially pure protein or polypeptide is isolated from the transfected or transformed cells as described in Example 30. The concentration of protein in the final preparation is adjusted, for example, by concentration on an Amicon filter device, to the level of a few micrograms/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows:

#### A. Monoclonal Antibody Production by Hybridoma Fusion

Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, G. and Milstein, C., Nature 256:495 (1975) or derivative methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein or peptides derived therefrom over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as Elisa, as originally described by Engvall, E., Meth. Enzymol. 70:419 (1980), and derivative methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. et al. Basic Methods in Molecular Biology Elsevier, New York. Section 21-2.

## B. Polyclonal Antibody Production by Immunization

Polyclonal antiserum containing antibodies to heterogenous epitopes of a single protein can be prepared by immunizing suitable animals with the expressed protein or peptides derived therefrom described above, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than others and may require the use of carriers and adjuvant. Also, host animals vary in response to site of inoculations and dose, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis, J. et al. J. Clin. Endocrinol. Metab. 33:988-991 (1971).

Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, O. et al., Chap. 19 in: Handbook of Experimental Immunology D. Wier (ed) Blackwell (1973). Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12 µM). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: Manual of Clinical Immunology, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D.C. (1980).

Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies may also be used in therapeutic compositions for killing cells expressing the protein or reducing the levels of the protein in the body.

## V. Use of Extended cDNAs or Portions Thereof as Reagents

The extended cDNAs of the present invention may be used as reagents in isolation procedures, diagnostic assays, and forensic procedures. For example, sequences from the extended cDNAs (or genomic DNAs obtainable therefrom) may be detectably labeled and used as probes to isolate other sequences capable of hybridizing to them. In addition, sequences from the extended cDNAs (or genomic DNAs obtainable therefrom) may be used to design PCR primers to be used in isolation, diagnostic, or forensic procedures.

#### **EXAMPLE 41**

## Preparation of PCR Primers and Amplification of DNA

The extended cDNAs (or genomic DNAs obtainable therefrom) may be used to prepare PCR primers for a variety of applications, including isolation procedures for cloning nucleic acids capable of hybridizing to such sequences, diagnostic techniques and forensic techniques. The PCR primers are at least 10 bases, and preferably at least 12, 15, or 17 bases in length. More preferably, the PCR primers are at least 20-30 bases in length. In some embodiments, the PCR primers may be more than 30 bases in length. It is preferred that the primer pairs have approximately the same G/C

ratio, so that melting temperatures are approximately the same. A variety of PCR techniques are familiar to those skilled in the art. For a review of PCR technology, see Molecular Cloning to Genetic Engineering White, B.A. Ed. in Methods in Molecular Biology 67: Humana Press, Totowa 1997. In each of these PCR procedures, PCR primers on either side of the nucleic acid sequences to be amplified are added to a suitably prepared nucleic acid sample along with dNTPs and a thermostable polymerase such as Taq polymerase, Pfu polymerase, or Vent polymerase. The nucleic acid in the sample is denatured and the PCR primers are specifically hybridized to complementary nucleic acid sequences in the sample. The hybridized primers are extended. Thereafter, another cycle of denaturation, hybridization, and extension is initiated. The cycles are repeated multiple times to produce an amplified fragment containing the nucleic acid sequence between the primer sites.

10 EXAMPLE 42

#### Use of Extended cDNAs as Probes

Probes derived from extended cDNAs or portions thereof (or genomic DNAs obtainable therefrom) may be labeled with detectable labels familiar to those skilled in the art, including radioisotopes and non-radioactive labels, to provide a detectable probe. The detectable probe may be single stranded or double stranded and may be made using techniques known in the art, including in vitro transcription, nick translation, or kinase reactions. A nucleic acid sample containing a sequence capable of hybridizing to the labeled probe is contacted with the labeled probe. If the nucleic acid in the sample is double stranded, it may be denatured prior to contacting the probe. In some applications, the nucleic acid sample may be immobilized on a surface such as a nitrocellulose or nylon membrane. The nucleic acid sample may comprise nucleic acids obtained from a variety of sources, including genomic DNA, cDNA libraries, RNA, or tissue samples.

Procedures used to detect the presence of nucleic acids capable of hybridizing to the detectable probe include well known techniques such as Southern blotting, Northern blotting, dot blotting, colony hybridization, and plaque hybridization. In some applications, the nucleic acid capable of hybridizing to the labeled probe may be cloned into vectors such as expression vectors, sequencing vectors, or in vitro transcription vectors to facilitate the characterization and expression of the hybridizing nucleic acids in the sample. For example, such techniques may be used to isolate and clone sequences in a genomic library or cDNA library which are capable of hybridizing to the detectable probe as described in Example 30 above.

PCR primers made as described in Example 41 above may be used in forensic analyses, such as the DNA fingerprinting techniques described in Examples 43-47 below. Such analyses may utilize detectable probes or primers based on the sequences of the extended cDNAs isolated using the 5' ESTs (or genomic DNAs obtainable therefrom).

#### **EXAMPLE 43**

#### Forensic Matching by DNA Sequencing

In one exemplary method, DNA samples are isolated from forensic specimens of, for example, hair, semen, blood or skin cells by conventional methods. A panel of PCR primers based on a number of the extended cDNAs (or

genomic DNAs obtainable therefrom), is then utilized in accordance with Example 41 to amplify DNA of approximately 100-200 bases in length from the forensic specimen. Corresponding sequences are obtained from a test subject. Each of these identification DNAs is then sequenced using standard techniques, and a simple database comparison determines the differences, if any, between the sequences from the subject and those from the sample. Statistically significant differences between the suspect's DNA sequences and those from the sample conclusively prove a lack of identity. This lack of identity can be proven, for example, with only one sequence. Identity, on the other hand, should be demonstrated with a large number of sequences, all matching. Preferably, a minimum of 50 statistically identical sequences of 100 bases in length are used to prove identity between the suspect and the sample.

#### **EXAMPLE 44**

10

#### Positive Identification by DNA Sequencing

The technique outlined in the previous example may also be used on a larger scale to provide a unique fingerprint-type identification of any individual. In this technique, primers are prepared from a large number of sequences from Table IV and the appended sequence listing. Preferably, 20 to 50 different primers are used. These primers are used to obtain a corresponding number of PCR-generated DNA segments from the individual in question in accordance with Example 41. Each of these DNA segments is sequenced, using the methods set forth in Example 43. The database of sequences generated through this procedure uniquely identifies the individual from whom the sequences were obtained. The same panel of primers may then be used at any later time to absolutely correlate tissue or other biological specimen with that individual.

#### **EXAMPLE 45**

20

#### Southern Blot Forensic Identification

The procedure of Example 44 is repeated to obtain a panel of at least 10 amplified sequences from an individual and a specimen. Preferably, the panel contains at least 50 amplified sequences. More preferably, the panel contains 100 amplified sequences. In some embodiments, the panel contains 200 amplified sequences. This PCR-generated DNA is then digested with one or a combination of, preferably, four base specific restriction enzymes. Such enzymes are commercially available and known to those of skill in the art. After digestion, the resultant gene fragments are size separated in multiple duplicate wells on an agarose gel and transferred to nitrocellulose using Southern blotting techniques well known to those with skill in the art. For a review of Southern blotting see Davis et al. (Basic Methods in Molecular Biology, 1986, Elsevier Press. pp 62-65).

A panel of probes based on the sequences of the extended cDNAs (or genomic DNAs obtainable therefrom), or fragments thereof of at least 10 bases, are radioactively or colorimetrically labeled using methods known in the art, such as nick translation or end labeling, and hybridized to the Southern blot using techniques known in the art (Davis et al., <a href="supra">supra</a>). Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). More preferably, the probe comprises at least 20-30 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). In some embodiments, the probe comprises more than 30

nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). In other embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom).

Preferably, at least 5 to 10 of these labeled probes are used, and more preferably at least about 20 or 30 are 5 used to provide a unique pattern. The resultant bands appearing from the hybridization of a large sample of extended cDNAs (or genomic DNAs obtainable therefrom) will be a unique identifier. Since the restriction enzyme cleavage will be different for every individual, the band pattern on the Southern blot will also be unique. Increasing the number of extended cDNA probes will provide a statistically higher level of confidence in the identification since there will be an increased number of sets of bands used for identification.

10

25

#### **EXAMPLE 46**

#### **Dot Blot Identification Procedure**

Another technique for identifying individuals using the extended cDNA sequences disclosed herein utilizes a dot blot hybridization technique.

Genomic DNA is isolated from nuclei of subject to be identified. Oliponucleotide probes of approximately 30 bp 15 in length are synthesized that correspond to at least 10, preferably 50 sequences from the extended cDNAs or genomic DNAs obtainable therefrom. The probes are used to hybridize to the genomic DNA through conditions known to those in the art. The oligonucleotides are end labeled with P32 using polynucleotide kinase (Pharmacia). Dot Blots are created by spotting the genomic DNA onto nitrocellulose or the like using a vacuum dot blot manifold (BioRad, Richmond California). The nitrocellulose filter containing the genomic sequences is baked or UV linked to the filter, prehybridized and 20 hybridized with labeled probe using techniques known in the art (Davis et al. supra). The <sup>32</sup>P labeled DNA fragments are sequentially hybridized with successively stringent conditions to detect minimal differences between the 30 bp sequence and the DNA. Tetramethylammonium chloride is useful for identifying clones containing small numbers of nucleotide mismatches (Wood et al., Proc. Natl. Acad. Sci. USA 82(6):1585-1588 (1985)). A unique pattern of dots distinguishes one individual from another individual.

Extended cDNAs or oligonucleotides containing at least 10 consecutive bases from these sequences can be used as probes in the following alternative fingerprinting technique. Preferably, the probe comprises at least 12, 15, or 17 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). More preferably, the probe comprises at least 20-30 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom). In some embodiments, the probe comprises more than 30 nucleotides from the extended cDNA (or genomic 30 DNAs obtainable therefrom). In other embodiments, the probe comprises at least 40, at least 50, at least 75, at least 100, at least 150, or at least 200 consecutive nucleotides from the extended cDNA (or genomic DNAs obtainable therefrom).

Preferably, a plurality of probes having sequences from different genes are used in the alternative fingerprinting technique. Example 47 below provides a representative alternative fingerprinting procedure in which the probes are derived from extended cDNAs.

#### **EXAMPLE 47**

5

## Alternative "Fingerprint" Identification Technique

20-mer oligonucleotides are prepared from a large number, e.g. 50, 100, or 200, of extended cDNA sequences (or genomic DNAs obtainable therefrom) using commercially available oligonucleotide services such as Genset, Paris, France. Cell samples from the test subject are processed for DNA using techniques well known to those with skill in the art. The nucleic acid is digested with restriction enzymes such as EcoRI and Xbal. Following digestion, samples are applied to wells for electrophoresis. The procedure, as known in the art, may be modified to accommodate polyacrylamide electrophoresis, however in this example, samples containing 5 ug of DNA are loaded into wells and separated on 0.8% agarose gels. The gels are transferred onto nitrocellulose using standard Southern blotting techniques.

10 ng of each of the oligonucleotides are pooled and end-labeled with P<sup>32</sup>. The nitrocellulose is prehybridized
with blocking solution and hybridized with the labeled probes. Following hybridization and washing, the nitrocellulose
filter is exposed to X-Omat AR X-ray film. The resulting hybridization pattern will be unique for each individual.

It is additionally contemplated within this example that the number of probe sequences used can be varied for additional accuracy or clarity.

The antibodies generated in Examples 30 and 40 above may be used to identify the tissue type or cell species from which a sample is derived as described above.

## **EXAMPLE 48**

# Identification of Tissue Types or Cell Species by Means of Labeled Tissue Specific Antibodies

Identification of specific tissues is accomplished by the visualization of tissue specific antigens by means of
antibody preparations according to Examples 30 and 40 which are conjugated, directly or indirectly to a detectable
marker. Selected labeled antibody species bind to their specific antigen binding partner in tissue sections, cell
suspensions, or in extracts of soluble proteins from a tissue sample to provide a pattern for qualitative or semiqualitative interpretation.

Antisera for these procedures must have a potency exceeding that of the native preparation, and for that

reason, antibodies are concentrated to a mg/ml level by isolation of the gamma globulin fraction, for example, by ionexchange chromatography or by ammonium sulfate fractionation. Also, to provide the most specific antisera, unwanted
antibodies, for example to common proteins, must be removed from the gamma globulin fraction, for example by means
of insoluble immunoabsorbents, before the antibodies are labeled with the marker. Either monoclonal or heterologous
antisera is suitable for either procedure.

20

### A. Immunohistochemical Techniques

Purified, high-titer antibodies, prepared as described above, are conjugated to a detectable marker, as described, for example, by Fudenberg, H., Chap. 26 in: Basic 503 Clinical Immunology, 3rd Ed. Lange, Los Altos, California (1980) or Rose, N. et al., Chap. 12 in: Methods in Immunodiagnosis, 2d Ed. John Wiley 503 Sons, New York (1980).

A fluorescent marker, either fluorescein or rhodamine, is preferred, but antibodies can also be labeled with an enzyme that supports a color producing reaction with a substrate, such as horseradish peroxidase. Markers can be added to tissue-bound antibody in a second step, as described below. Alternatively, the specific antitissue antibodies can be labeled with ferritin or other electron dense particles, and localization of the ferritin coupled antigen-antibody complexes achieved by means of an electron microscope. In yet another approach, the antibodies are radiolabeled, with, for example 1251, and detected by overlaying the antibody treated preparation with photographic emulsion.

Preparations to carry out the procedures can comprise monoclonal or polyclonal antibodies to a single protein or peptide identified as specific to a tissue type, for example, brain tissue, or antibody preparations to several antigenically distinct tissue specific antigens can be used in panels, independently or in mixtures, as required.

Tissue sections and cell suspensions are prepared for immunohistochemical examination according to common histological techniques. Multiple cryostat sections (about 4 µm, unfixed) of the unknown tissue and known control, are mounted and each slide covered with different dilutions of the antibody preparation. Sections of known and unknown tissues should also be treated with preparations to provide a positive control, a negative control, for example, pre-immune sera, and a control for non-specific staining, for example, buffer.

Treated sections are incubated in a humid chamber for 30 min at room temperature, rinsed, then washed in buffer for 30-45 min. Excess fluid is blotted away, and the marker developed.

If the tissue specific antibody was not labeled in the first incubation, it can be labeled at this time in a second antibody-antibody reaction, for example, by adding fluorescein- or enzyme-conjugated antibody against the immunoglobulin class of the antiserum-producing species, for example, fluorescein labeled antibody to mouse IgG. Such 25 labeled sera are commercially available.

The antigen found in the tissues by the above procedure can be quantified by measuring the intensity of color or fluorescence on the tissue section, and calibrating that signal using appropriate standards.

## B. Identification of Tissue Specific Soluble Proteins

The visualization of tissue specific proteins and identification of unknown tissues from that procedure is

30 carried out using the labeled antibody reagents and detection strategy as described for immunohistochemistry; however
the sample is prepared according to an electrophoretic technique to distribute the proteins extracted from the tissue in
an orderly array on the basis of molecular weight for detection.

A tissue sample is homogenized using a Virtis apparatus; cell suspensions are disrupted by Dounce homogenization or osmotic lysis, using detergents in either case as required to disrupt cell membranes, as is the practice

r Jan

in the art. Insoluble cell components such as nuclei, microsomes, and membrane fragments are removed by ultracentrifugation, and the soluble protein-containing fraction concentrated if necessary and reserved for analysis.

A sample of the soluble protein solution is resolved into individual protein species by conventional SDS polyacrylamide electrophoresis as described, for example, by Davis, L. et al., Section 19-2 in: Basic Methods in 5 Molecular Biology (P. Leder, ed), Elsevier, New York (1986), using a range of amounts of polyacrylamide in a set of gels to resolve the entire molecular weight range of proteins to be detected in the sample. A size marker is run in parallel for purposes of estimating molecular weights of the constituent proteins. Sample size for analysis is a convenient volume of from 5 to 55  $\mu$ l, and containing from about 1 to 100  $\mu$ g protein. An aliquot of each of the resolved proteins is transferred by blotting to a nitrocellulose filter paper, a process that maintains the pattern of resolution. Multiple copies 10 are prepared. The procedure, known as Western Blot Analysis, is well described in Davis, L. et al., (above) Section 19-3. One set of nitrocellulose blots is stained with Coomassie Blue dye to visualize the entire set of proteins for comparison with the antibody bound proteins. The remaining nitrocellulose filters are then incubated with a solution of one or more specific antisera to tissue specific proteins prepared as described in Examples 30 and 40. In this procedure, as in procedure A above, appropriate positive and negative sample and reagent controls are run.

In either procedure A or B, a detectable label can be attached to the primary tissue antigen-primary antibody complex according to various strategies and permutations thereof. In a straightforward approach, the primary specific antibody can be labeled; alternatively, the unlabeled complex can be bound by a labeled secondary anti-IgG antibody. In other approaches, either the primary or secondary antibody is conjugated to a biotin molecule, which can, in a subsequent step, bind an avidin conjugated marker. According to yet another strategy, enzyme labeled or radioactive 20 protein A, which has the property of binding to any IgG, is bound in a final step to either the primary or secondary antibody.

The visualization of tissue specific antigen binding at levels above those seen in control tissues to one or more tissue specific antibodies, prepared from the gene sequences identified from extended cDNA sequences, can identify tissues of unknown origin, for example, forensic samples, or differentiated tumor tissue that has metastasized to foreign 25 bodily sites.

In addition to their applications in forensics and identification, extended cDNAs (or genomic DNAs obtainable therefrom) may be mapped to their chromosomal locations. Example 49 below describes radiation hybrid (RH) mapping of human chromosomal regions using extended cDNAs. Example 50 below describes a representative procedure for mapping an extended cDNA (or a genomic DNA obtainable therefrom) to its location on a human chromosome. Example 30 51 below describes mapping of extended cDNAs (or genomic DNAs obtainable therefrom) on metaphase chromosomes by Fluorescence In Situ Hybridization (FISH).

## **EXAMPLE 49**

Radiation hybrid mapping of Extended cDNAs to the human genome

Radiation hybrid (RH) mapping is a somatic cell genetic approach that can be used for high resolution mapping of the human genome. In this approach, cell lines containing one or more human chromosomes are lethally irradiated, breaking each chromosome into fragments whose size depends on the radiation dose. These fragments are rescued by fusion with cultured rodent cells, yielding subclones containing different portions of the human genome. This technique is described by Benham et al. (*Genomics* 4:509-517, 1989) and Cox et al., (*Science* 250:245-250, 1990). The random and independent nature of the subclones permits efficient mapping of any human genome marker. Human DNA isolated from a panel of 80-100 cell lines provides a mapping reagent for ordering extended cDNAs (or genomic DNAs obtainable therefrom). In this approach, the frequency of breakage between markers is used to measure distance, allowing construction of fine resolution maps as has been done using conventional ESTs (Schuler et al., *Science* 274:540-546, 1996).

RH mapping has been used to generate a high-resolution whole genome radiation hybrid map of human chromosome 17q22-q25.3 across the genes for growth hormone (GH) and thyr idine kinase (TK) (Foster et al., *Genomics* 33:185-192, 1996), the region surrounding the Gorlin syndrome gene (Obermayr et al., *Eur. J. Hum. Genet.* 4:242-245, 1996), 60 loci covering the entire short arm of chromosome 12 (Raeymaekers et al., *Genomics* 29:170-178, 1995), the region of human chromosome 22 containing the neurofibromatosis type 2 locus (Frazer et al., *Genomics* 14:574-584, 1992) and 13 loci on the long arm of chromosome 5 (Warrington et al., *Genomics* 11:701-708, 1991).

## **EXAMPLE 50**

## Mapping of Extended cDNAs to Human

#### Chromosomes using PCR techniques

Extended cDNAs (or genomic DNAs obtainable therefrom) may be assigned to human chromosomes using PCR based methodologies. In such approaches, oligonucleotide primer pairs are designed from the extended cDNA sequence (or the sequence of a genomic DNA obtainable therefrom) to minimize the chance of amplifying through an intron. Preferably, the oligonucleotide primers are 18-23 bp in length and are designed for PCR amplification. The creation of PCR primers from known sequences is well known to those with skill in the art. For a review of PCR technology see Erlich, H.A., PCR Technology; Principles and Applications for DNA Amplification. 1992. W.H. Freeman and Co., New York.

The primers are used in polymerase chain reactions (PCR) to amplify templates from total human genomic DNA. PCR conditions are as follows: 60 ng of genomic DNA is used as a template for PCR with 80 ng of each oligonucleotide primer, 0.6 unit of Taq polymerase, and 1 µCu of a <sup>32</sup>P-labeled deoxycytidine triphosphate. The PCR is performed in a microplate thermocycler (Techne) under the following conditions: 30 cycles of 94°C, 1.4 min; 55°C, 2 min; and 72°C, 2 min; with a final extension at 72°C for 10 min. The amplified products are analyzed on a 6% polyacrylamide sequencing gel and visualized by autoradiography. If the length of the resulting PCR product is identical to the distance between the ends of the primer sequences in the extended cDNA from which the primers are derived, then the PCR reaction is repeated with DNA templates from two panels of human-rodent somatic cell hybrids, BIOS

PCRable DNA (BIOS Corporation) and NIGMS Human-Rodent Somatic Cell Hybrid Mapping Panel Number 1 (NIGMS, Camden, NJ).

PCR is used to screen a series of somatic cell hybrid cell lines containing defined sets of human chromosomes for the presence of a given extended cDNA (or genomic DNA obtainable therefrom). DNA is isolated from the somatic hybrids and used as starting templates for PCR reactions using the primer pairs from the extended cDNAs (or genomic DNAs obtainable therefrom). Only those somatic cell hybrids with chromosomes containing the human gene corresponding to the extended cDNA (or genomic DNA obtainable therefrom) will yield an amplified fragment. The extended cDNAs (or genomic DNAs obtainable therefrom) are assigned to a chromosome by analysis of the segregation pattern of PCR products from the somatic hybrid DNA templates. The single human chromosome present in all cell hybrids that give rise to an amplified fragment is the chromosome containing that extended cDNA (or genomic DNA obtainable therefrom). For a review of techniques and analysis of results from somatic cell gene mapping experiments. (See Ledbetter et al., Genomics 6:475-481 (1990).)

Alternatively, the extended cDNAs (or genomic DNAs obtainable therefrom) may be mapped to individual chromosomes using FISH as described in Example 51 below.

15

#### **EXAMPLE 51**

## Mapping of Extended 5' ESTs to Chromosomes

#### Using Fluorescence in situ Hybridization

Fluorescence in situ hybridization allows the extended cDNA (or genomic DNA obtainable therefrom) to be mapped to a particular location on a given chromosome. The chromosomes to be used for fluorescence in situ hybridization techniques may be obtained from a variety of sources including cell cultures, tissues, or whole blood.

In a preferred embodiment, chromosomal localization of an extended cDNA (or genomic DNA obtainable therefrom) is obtained by FISH as described by Cherif et al. (*Proc. Natl. Acad. Sci. U.S.A.*, 87:6639-6643, 1990).

Metaphase chromosomes are prepared from phytohemagglutinin (PHA)-stimulated blood cell donors. PHA-stimulated lymphocytes from healthy males are cultured for 72 h in RPMI-1640 medium. For synchronization, methotrexate (10 µM) is added for 17 h, followed by addition of 5-bromodeoxyuridine (5-BudR, 0.1 mM) for 6 h. Colcemid (1 µg/ml) is added for the last 15 min before harvesting the cells. Cells are collected, washed in RPMI, incubated with a hypotonic solution of KCI (75 mM) at 37°C for 15 min and fixed in three changes of methanol:acetic acid (3:1). The cell suspension is dropped onto a glass slide and air dried. The extended cDNA (or genomic DNA obtainable therefrom) is labeled with biotin-16 dUTP by nick translation according to the manufacturer's instructions (Bethesda Research

Laboratories, Bethesda, MD), purified using a Sephadex G-50 column (Pharmacia, Upssala, Sweden) and precipitated. Just prior to hybridization, the DNA pellet is dissolved in hybridization buffer (50% formamide, 2 X SSC, 10% dextran sulfate, 1 mg/ml sonicated salmon sperm DNA, pH 7) and the probe is denatured at 70°C for 5-10 min.

Slides kept at -20°C are treated for 1 h at 37°C with RNase A (100  $\mu$ g/ml), rinsed three times in 2 X SSC and dehydrated in an ethanol series. Chromosome preparations are denatured in 70% formamide, 2 X SSC for 2 min at

WO 99/31236

15

70°C, then dehydrated at 4°C. The slides are treated with proteinase K (10 μg/100 ml in 20 mM Tris-HCl, 2 mM CaCl<sub>2</sub>) at 37°C for 8 min and dehydrated. The hybridization mixture containing the probe is placed on the slide, covered with a coverslip, sealed with rubber cement and incubated overnight in a humid chamber at 37°C. After hybridization and post-hybridization washes, the biotinylated probe is detected by avidin-FITC and amplified with additional layers of biotinylated goat anti-avidin and avidin-FITC. For chromosomal localization, fluorescent R-bands are obtained as previously described (Cherif et al., supra.). The slides are observed under a LEICA fluorescence microscope (DMRXA). Chromosomes are counterstained with propidium iodide and the fluorescent signal of the probe appears as two symmetrical yellow-green spots on both chromatids of the fluorescent R-band chromosome (red). Thus, a particular extended cDNA (or genomic DNA obtainable therefrom) may be localized to a particular cytogenetic R-band on a given

Once the extended cDNAs (or genomic DNAs obtainable therefrom) have been assigned to particular chromosomes using the techniques described in Examples 49-51 above, they may be utilized to construct a high resolution map of the chromosomes on which they are located or to identify the chromosomes in a sample.

## **EXAMPLE 52**

## Use of Extended cDNAs to Construct or Expand Chromosome Maps

Chromosome mapping involves assigning a given unique sequence to a particular chromosome as described above. Once the unique sequence has been mapped to a given chromosome, it is ordered relative to other unique sequences located on the same chromosome. One approach to chromosome mapping utilizes a series of yeast artificial chromosomes (YACs) bearing several thousand long inserts derived from the chromosomes of the organism from which the extended cDNAs (or genomic DNAs obtainable therefrom) are obtained. This approach is described in Ramaiah Nagaraja et al. Genome Research 7:210-222, March 1997. Briefly, in this approach each chromosome is broken into overlapping pieces which are inserted into the YAC vector. The YAC inserts are screened using PCR or other methods to determine whether they include the extended cDNA (or genomic DNA obtainable therefrom) whose position is to be determined. Once an insert has been found which includes the extended cDNA (or genomic DNA obtainable therefrom), the insert can be analyzed by PCR or other methods to determine whether the insert also contains other sequences known to be on the chromosome or in the region from which the extended cDNA (or genomic DNA obtainable therefrom) was derived. This process can be repeated for each insert in the YAC library to determine the location of each of the extended cDNAs (or genomic DNAs obtainable therefrom) relative to one another and to other known chromosomal markers. In this way, a high resolution map of the distribution of numerous unique markers along each of the organisms 30 chromosomes may be obtained.

As described in Example 53 below extended cDNAs (or genomic DNAs obtainable therefrom) may also be used to identify genes associated with a particular phenotype, such as hereditary disease or drug response.

#### **EXAMPLE 53**

Identification of genes associated with hereditary diseases or drug response

This example illustrates an approach useful for the association of extended cDNAs (or genomic DNAs obtainable therefrom) with particular phenotypic characteristics. In this example, a particular extended cDNA (or genomic DNA obtainable therefrom) is used as a test probe to associate that extended cDNA (or genomic DNA obtainable therefrom) with a particular phenotypic characteristic.

Extended cDNAs (or genomic DNAs obtainable therefrom) are mapped to a particular location on a human chromosome using techniques such as those described in Examples 49 and 50 or other techniques known in the art. A search of Mendelian Inheritance in Man (V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library) reveals the region of the human chromosome which contains the extended cDNA (or genomic DNA obtainable therefrom) to be a very gene rich region containing several known genes and several 10 diseases or phenotypes for which genes have not been identified. The gene corresponding to this extended cDNA (or genomic DNA obtainable therefrom) thus becomes an immediate candidate for each of these genetic diseases.

Cells from patients with these diseases or phenotypes are isolated and expanded in culture. PCR primers from the extended cDNA (or genomic DNA obtainable therefrom) are used to screen genomic DNA, mRNA or cDNA obtained from the patients. Extended cDNAs (or genomic DNAs obtainable therefrom) that are not amplified in the patients can 15 be positively associated with a particular disease by further analysis. Alternatively, the PCR analysis may yield fragments of different lengths when the samples are derived from an individual having the phenotype associated with the disease than when the sample is derived from a healthy individual, indicating that the gene containing the extended cDNA may be responsible for the genetic disease.

## VI. Use of Extended cDNAs (or genomic DNAs obtainable therefrom) to Construct Vectors

20 The present extended cDNAs (or genomic DNAs obtainable therefrom) may also be used to construct secretion vectors capable of directing the secretion of the proteins encoded by genes inserted in the vectors. Such secretion vectors may facilitate the purification or enrichment of the proteins encoded by genes inserted therein by reducing the number of background proteins from which the desired protein must be purified or enriched. Exemplary secretion vectors are described in Example 54 below.

25

30

## **EXAMPLE 54**

## **Construction of Secretion Vectors**

The secretion vectors of the present invention include a promoter capable of directing gene expression in the host cell, tissue, or organism of interest. Such promoters include the Rous Sarcoma Virus promoter, the SV40 promoter, the human cytomegalovirus promoter, and other promoters familiar to those skilled in the art.

A signal sequence from an extended cDNA (or genomic DNA obtainable therefrom), such as one of the signal sequences in SEO ID NOs: 40-140 and 242-377 as defined in Table IV above, is operably linked to the promoter such that the mRNA transcribed from the promoter will direct the translation of the signal peptide. The host cell, tissue, or organism may be any cell, tissue, or organism which recognizes the signal peptide encoded by the signal sequence in the

extended cDNA (or genomic DNA obtainable therefrom). Suitable hosts include mammalian cells, tissues or organisms; avian cells, tissues, or organisms, insect cells, tissues or organisms, or yeast.

In addition, the secretion vector contains cloning sites for inserting genes encoding the proteins which are to be secreted. The cloning sites facilitate the cloning of the insert gene in frame with the signal sequence such that a fusion 5 protein in which the signal peptide is fused to the protein encoded by the inserted gene is expressed from the mRNA transcribed from the promoter. The signal peptide directs the extracellular secretion of the fusion protein.

The secretion vector may be DNA or RNA and may integrate into the chromosome of the host, be stably maintained as an extrachromosomal replicon in the host, be an artificial chromosome, or be transiently present in the host. Many nucleic acid backbones suitable for use as secretion vectors are known to those skilled in the art, including 10 retroviral vectors, SV40 vectors, Bovine Papilloma Virus vectors, yeast integrating plasmids, yeast episomal plasmids, yeast artificial chromosomes, human artificial chromosomes, P element vectors, baculovirus vectors, or bacterial plasmids capable of being transiently introduced into the host.

The secretion vector may also contain a polyA signal such that the polyA signal is located downstream of the gene inserted into the secretion vector.

After the gene encoding the protein for which secretion is desired is inserted into the secretion vector, the secretion vector is introduced into the host cell, tissue, or organism using calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection, viral particles or as naked DNA. The protein encoded by the inserted gene is then purified or enriched from the supernatant using conventional techniques such as ammonium sulfate precipitation, immunoprecipitation, immunochromatography, size exclusion chromatography, ion exchange 20 chromatography, and hplc. Alternatively, the secreted protein may be in a sufficiently enriched or pure state in the supernatant or growth media of the host to permit it to be used for its intended purpose without further enrichment.

The signal sequences may also be inserted into vectors designed for gene therapy. In such vectors, the signal sequence is operably linked to a promoter such that mRNA transcribed from the promoter encodes the signal peptide. A cloning site is located downstream of the signal sequence such that a gene encoding a protein whose secretion is 25 desired may readily be inserted into the vector and fused to the signal sequence. The vector is introduced into an appropriate host cell. The protein expressed from the promoter is secreted extracellularly, thereby producing a therapeutic effect.

The extended cDNAs or 5' ESTs may also be used to clone sequences located upstream of the extended cDNAs or 5' ESTs which are capable of regulating gene expression, including promoter sequences, enhancer sequences, and 30 other upstream sequences which influence transcription or translation levels. Once identified and cloned, these upstream regulatory sequences may be used in expression vectors designed to direct the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative fashion. Example 55 describes a method for cloning sequences upstream of the extended cDNAs or 5' ESTs.

## Use of Extended cDNAs or 5' ESTs to Clone Upstream

## Sequences from Genomic DNA

Sequences derived from extended cDNAs or 5' ESTs may be used to isolate the promoters of the corresponding genes using chromosome walking techniques. In one chromosome walking technique, which utilizes the GenomeWalker<sup>TM</sup> kit available from Clontech, five complete genomic DNA samples are each digested with a different restriction enzyme which has a 6 base recognition site and leaves a blunt end. Following digestion, oligonucleotide adapters are ligated to each end of the resulting genomic DNA fragments.

For each of the five genomic DNA libraries, a first PCR reaction is performed according to the manufacturer's instructions using an outer adaptor primer provided in the kit and an outer gene specific primer. The gene specific primer should be selected to be specific for the extended cDNA or 5' EST of interest and should have a melting temperature, length, and location in the extended cDNA or ' EST which is consistent with its use in PCR reactions. Each first PCR reaction contains 5ng of genomic DNA, 5 \(\mu\)I of 10X Tth reaction buffer, 0.2 mM of each dNTP, 0.2 \(\mu\)M each of outer adaptor primer and outer gene specific primer, 1.1 mM of Mg(0Ac)<sub>2</sub>, and 1 \(\mu\)I of the Tth polymerase 50X mix in a total volume of 50 \(\mu\)I. The reaction cycle for the first PCR reaction is as follows: 1 min @ 94°C / 2 sec @ 94°C, 3 min @ 72°C (7 cycles) / 2 sec @ 94°C, 3 min @ 67°C (32 cycles) / 5 min @ 67°C.

The product of the first PCR reaction is diluted and used as a template for a second PCR reaction according to the manufacturer's instructions using a pair of nested primers which are located internally on the amplicon resulting from the first PCR reaction. For example, 5 µl of the reaction product of the first PCR reaction mixture may be diluted 180 times. Reactions are made in a 50 µl volume having a composition identical to that of the first PCR reaction except the nested primers are used. The first nested primer is specific for the adaptor, and is provided with the GenomeWalker™ kit. The second nested primer is specific for the particular extended cDNA or 5' EST for which the promoter is to be cloned and should have a melting temperature, length, and location in the extended cDNA or 5' EST which is consistent with its use in PCR reactions. The reaction parameters of the second PCR reaction are as follows: 1 min @ 94°C / 2 sec @ 94°C, 3 min @ 67°C (25 cycles) / 5 min @ 67°C

The product of the second PCR reaction is purified, cloned, and sequenced using standard techniques.

Alternatively, two or more human genomic DNA libraries can be constructed by using two or more restriction enzymes.

The digested genomic DNA is cloned into vectors which can be converted into single stranded, circular, or linear DNA. A biotinylated oligonucleotide comprising at least 15 nucleotides from the extended cDNA or 5' EST sequence is hybridized to the single stranded DNA. Hybrids between the biotinylated oligonucleotide and the single stranded DNA containing the extended cDNA or EST sequence are isolated as described in Example 29 above. Thereafter, the single stranded DNA containing the extended cDNA or EST sequence is released from the beads and converted into double stranded DNA using a primer specific for the extended cDNA or 5' EST sequence or a primer corresponding to a sequence included in the cloning vector. The resulting double stranded DNA is transformed into bacteria. DNAs containing the 5' EST or extended cDNA sequences are identified by colony PCR or colony hybridization.

25

L.

Once the upstream genomic sequences have been cloned and sequenced as described above, prospective promoters and transcription start sites within the upstream sequences may be identified by comparing the sequences upstream of the extended cDNAs or 5' ESTs with databases containing known transcription start sites, transcription factor binding sites, or promoter sequences.

In addition, promoters in the upstream sequences may be identified using promoter reporter vectors as described in Example 56.

## **EXAMPLE 56**

## Identification of Promoters in Cloned Upstream Sequences

The genomic sequences upstream of the extended cDNAs or 5' ESTs are closed into a suitable promoter 10 reporter vector, such as the pSEAP-Basic, pSEAP-Enhancer, pßgal-Basic, pßgal-Enhancer, or pEGFP-1 Promoter Reporter vectors available from Clontech. Briefly, each of these promoter reporter vectors include multiple cloning sites positioned upstream of a reporter gene encoding a readily assayable protein such as secreted alkaline phosphatase,  $\beta$ galactosidase, or green fluorescent protein. The sequences upstream of the extended cDNAs or 5' ESTs are inserted into the cloning sites upstream of the reporter gene in both orientations and introduced into an appropriate host cell. The 15 level of reporter protein is assayed and compared to the level obtained from a vector which lacks an insert in the cloning site. The presence of an elevated expression level in the vector containing the insert with respect to the control vector indicates the presence of a promoter in the insert. If necessary, the upstream sequences can be cloned into vectors which contain an enhancer for augmenting transcription levels from weak promoter sequences. A significant level of expression above that observed with the vector lacking an insert indicates that a promoter sequence is present in the 20 inserted upstream sequence.

Appropriate host cells for the promoter reporter vectors may be chosen based on the results of the above described determination of expression patterns of the extended cDNAs and ESTs. For example, if the expression pattern analysis indicates that the mRNA corresponding to a particular extended cDNA or 5' EST is expressed in fibroblasts, the promoter reporter vector may be introduced into a human fibroblast cell line.

Promoter sequences within the upstream genomic DNA may be further defined by constructing nested deletions in the upstream DNA using conventional techniques such as Exonuclease III digestion. The resulting deletion fragments can be inserted into the promoter reporter vector to determine whether the deletion has reduced or obliterated promoter activity. In this way, the boundaries of the promoters may be defined. If desired, potential individual regulatory sites within the promoter may be identified using site directed mutagenesis or linker scanning to obliterate 30 potential transcription factor binding sites within the promoter individually or in combination. The effects of these mutations on transcription levels may be determined by inserting the mutations into the cloning sites in the promoter reporter vectors.

## **EXAMPLE 57**

15

Using the method described in Example 55 above with 5' ESTs, sequences upstream of several genes were obtained. Using the primer pairs GGG AAG ATG GAG ATA GTA TTG CCT G (SEQ ID NO:29) and CTG CCA TGT ACA TGA TAG AGA GAT TC (SEQ ID NO:30), the promoter having the internal designation P13H2 (SEQ ID NO:31) was obtained.

Using the primer pairs GTA CCA GGGG ACT GTG ACC ATT GC (SEQ ID NO:32) and CTG TGA CCA TTG CTC CCA AGA GAG (SEQ ID NO:33), the promoter having the internal designation P15B4 (SEQ ID NO:34) was obtained.

Using the primer pairs CTG GGA TGG AAG GCA CGG TA (SEO ID NO:35) and GAG ACC ACA CAG CTA GAC AA (SEQ ID NO:36), the promoter having the internal designation P29B6 (SEQ ID NO:37) was obtained.

Figure 8 provides a schematic description of the promoters isolated and the way they are assembled with the 10 corresponding 5' tags. The upstream sequences were screened for the presence of motifs resembling transcription factor binding sites or known transcription start sites using the computer program MatInspector release 2.0, August 1996.

Figure 9 describes the transcription factor binding sites present in each of these promoters. The columns labeled matrice provides the name of the MatInspector matrix used. The column labeled position provides the 5' postion of the promoter site. Numeration of the sequence starts from the transcription site as determined by matching the genomic sequence with the 5' EST sequence. The column labeled "orientation" indicates the DNA strand on which the site is found, with the + strand being the coding strand as determined by matching the genomic sequence with the sequence of the 5' EST. The column labeled "score" provides the MatInspector score found for this site. The column labeled "length" provides the length of the site in nucleotides. The column labeled "sequence" provides the sequence of 20 the site found.

The promoters and other regulatory sequences located upstream of the extended cDNAs or 5' ESTs may be used to design expression vectors capable of directing the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative manner. A promoter capable of directing the desired spatial, temporal, developmental, and quantitative patterns may be selected using the results of the expression analysis described in Example 26 above. For 25 example, if a promoter which confers a high level of expression in muscle is desired, the promoter sequence upstream of an extended cDNA or 5' EST derived from an mRNA which is expressed at a high level in muscle, as determined by the method of Example 26, may be used in the expression vector.

Preferably, the desired promoter is placed near multiple restriction sites to facilitate the cloning of the desired insert downstream of the promoter, such that the promoter is able to drive expression of the inserted gene. The 30 promoter may be inserted in conventional nucleic acid backbones designed for extrachromosomal replication, integration into the host chromosomes or transient expression. Suitable backbones for the present expression vectors include retroviral backbones, backbones from eukaryotic episomes such as SV40 or Bovine Papilloma Virus, backbones from bacterial episomes, or artificial chromosomes.

Preferably, the expression vectors also include a polyA signal downstream of the multiple restriction sites for directing the polyadenylation of mRNA transcribed from the gene inserted into the expression vector.

Following the identification of promoter sequences using the procedures of Examples 55-57, proteins which interact with the promoter may be identified as described in Example 58 below.

5

30

#### **EXAMPLE 58**

# Identification of Proteins Which Interact with Promoter Sequences, Upstream Regulatory Sequences, or mRNA

Sequences within the promoter region which are likely to bind transcription factors may be identified by homology to known transcription factor binding sites or through conventional mutagenesis or deletion analyses of reporter plasmids containing the promoter sequence. For example, deletions may be made in a reporter plasmid containing the promoter sequence of interest operably linked to an assayable reporter gene. The reporter plasmids carrying various deletions within the promoter region are transfected into an appropriate host cell and the effects of the deletions on expression levels is assessed. Transcription factor binding sites within the regions in which deletions reduce expression levels may be further localized using site directed mutagenesis, linker scanning analysis, or other techniques familiar to those skilled in the art. Nucleic acids encoding proteins which interact with sequences in the promoter may be identified using one-hybrid systems such as those described in the manual accompanying the Matchmaker One-Hybrid System kit available from Clontech (Catalog No. K1603-1). Briefly, the Matchmaker One-hybrid system is used as follows. The target sequence for which it is desired to identify binding proteins is cloned upstream of a selectable reporter gene and integrated into the yeast genome. Preferably, multiple copies of the target sequences are inserted into the reporter plasmid in tandem.

A library comprised of fusions between cDNAs to be evaluated for the ability to bind to the promoter and the activation domain of a yeast transcription factor, such as GAL4, is transformed into the yeast strain containing the integrated reporter sequence. The yeast are plated on selective media to select cells expressing the selectable marker linked to the promoter sequence. The colonies which grow on the selective media contain genes encoding proteins which bind the target sequence. The inserts in the genes encoding the fusion proteins are further characterized by sequencing. In addition, the inserts may be inserted into expression vectors or in vitro transcription vectors. Binding of the polypeptides encoded by the inserts to the promoter DNA may be confirmed by techniques familiar to those skilled in the art, such as gel shift analysis or DNAse protection analysis.

## VII. Use of Extended cDNAs (or Genomic DNAs Obtainable Therefrom) in Gene Therapy

The present invention also comprises the use of extended cDNAs (or genomic DNAs obtainable therefrom) in gene therapy strategies, including antisense and triple helix strategies as described in Examples 57 and 58 below. In antisense approaches, nucleic acid sequences complementary to an mRNA are hybridized to the mRNA intracellularly, thereby blocking the expression of the protein encoded by the mRNA. The antisense sequences may prevent gene expression through a variety of mechanisms. For example, the antisense sequences may inhibit the ability of ribosomes

to translate the mRNA. Alternatively, the antisense sequences may block transport of the mRNA from the nucleus to the cytoplasm, thereby limiting the amount of mRNA available for translation. Another mechanism through which antisense sequences may inhibit gene expression is by interfering with mRNA splicing. In yet another strategy, the antisense nucleic acid may be incorporated in a ribozyme capable of specifically cleaving the target mRNA.

5

25

#### **EXAMPLE 59**

## Preparation and Use of Antisense Oligonucleotides

The antisense nucleic acid molecules to be used in gene therapy may be either DNA or RNA sequences. They may comprise a sequence complementary to the sequence of the extended cDNA (or genomic DNA obtainable therefrom). The antisense nucleic acids should have a length and melting temperature sufficient to permit formation of an 10 intracellular duplex having sufficient stability to inhibit the expression of the mRNA in the duplex. Strategies for designing antisense nucleic acids suitable for use in gene therapy are disclosed in Green et al., Ann. Rev. Biochem. 55:569-597 (1986) and Izant and Weintraub, Cell 36:1007-1015 (1984).

In some strategies, antisense molecules are obtained from a nucleotide sequence encoding a protein by reversing the orientation of the coding region with respect to a promoter so as to transcribe the opposite strand from 15 that which is normally transcribed in the cell. The antisense molecules may be transcribed using in vitro transcription systems such as those which employ T7 or SP6 polymerase to generate the transcript. Another approach involves transcription of the antisense nucleic acids in vivo by operably linking DNA containing the antisense sequence to a promoter in an expression vector.

Alternatively, oligonucleotides which are complementary to the strand normally transcribed in the cell may be 20 synthesized in vitro. Thus, the antisense nucleic acids are complementary to the corresponding mRNA and are capable of hybridizing to the mRNA to create a duplex. In some embodiments, the antisense sequences may contain modified sugar phosphate backbones to increase stability and make them less sensitive to RNase activity. Examples of modifications suitable for use in antisense strategies are described by Rossi et al., Pharmacol. Ther. 50(2):245-254, (1991).

Various types of antisense oligonucleotides complementary to the sequence of the extended cDNA (or genomic DNA obtainable therefrom) may be used. In one preferred embodiment, stable and semi-stable antisense oligonucleotides described in International Application No. PCT W094/23026 are used. In these moleucles, the 3' end or both the 3' and 5' ends are engaged in intramolecular hydrogen bonding between complementary base pairs. These molecules are better able to withstand exonuclease attacks and exhibit increased stability compared to conventional antisense 30 oligonucleotides.

In another preferred embodiment, the antisense oligodeoxynucleotides against herpes simplex virus types 1 and 2 described in International Application No. WO 95/04141.

In yet another preferred embodiment, the covalently cross-linked antisense oligonucleotides described in International Application No. WO 96/31523 are used. These double- or single-stranded oligonucleotides comprise one or more, respectively, inter- or intra-oligonucleotide covalent cross-linkages, wherein the linkage consists of an amide bond between a primary amine group of one strand and a carboxyl group of the other strand or of the same strand, respectively, the primary amine group being directly substituted in the 2' position of the strand nucleotide monosaccharide ring, and the carboxyl group being carried by an aliphatic spacer group substituted on a nucleotide or nucleotide analog of the other strand or the same strand, respectively.

The antisense oligodeoxynucleotides and oligonucleotides disclosed in International Application No. WO
92/18522 may also be used. These molecules are stable to degradation and contain at least one transcription control
recognition sequence which binds to control proteins and are effective as decoys therefor. These molecules may contain
"hairpin" structures, "dumbbell" structures, "modified dumbbell" structures, "cross-linked" decoy structures and "loop"

10 structures.

In another preferred embodiment, the cyclic double-stranded oligonucleotides described in European Patent Application No. 0 572 287 A2 are used. These ligated oligonucleotide "dumbbells" contain the binding site for a transcription factor and inhibit expression of the gene under control of the transcription factor by sequestering the factor.

15

Use of the closed antisense oligonucleotides disclosed in International Application No. WO 92/19732 is also contemplated. Because these molecules have no free ends, they are more resistant to degradation by exonucleases than are conventional oligonucleotides. These oligonucleotides may be multifunctional, interacting with several regions which are not adjacent to the target mRNA.

The appropriate level of antisense nucleic acids required to inhibit gene expression may be determined using in vitro expression analysis. The antisense molecule may be introduced into the cells by diffusion, injection, infection or transfection using procedures known in the art. For example, the antisense nucleic acids can be introduced into the body as a bare or naked oligonucleotide, oligonucleotide encapsulated in lipid, oligonucleotide sequence encapsidated by viral protein, or as an oligonucleotide operably linked to a promoter contained in an expression vector. The expression vector may be any of a variety of expression vectors known in the art, including retroviral or viral vectors, vectors capable of extrachromosomal replication, or integrating vectors. The vectors may be DNA or RNA.

The antisense molecules are introduced onto cell samples at a number of different concentrations preferably between 1x10<sup>-10</sup>M to 1x10<sup>-4</sup>M. Once the minimum concentration that can adequately control gene expression is identified, the optimized dose is translated into a dosage suitable for use in vivo. For example, an inhibiting concentration in culture of 1x10<sup>-7</sup> translates into a dose of approximately 0.6 mg/kg bodyweight. Levels of oligonucleotide approaching 100 mg/kg bodyweight or higher may be possible after testing the toxicity of the oligonucleotide in laboratory animals. It is additionally contemplated that cells from the vertebrate are removed, treated with the antisense oligonucleotide, and reintroduced into the vertebrate.

It is further contemplated that the antisense oligonucleotide sequence is incorporated into a ribozyme sequence to enable the antisense to specifically bind and cleave its target mRNA. For technical applications of ribozyme and antisense oligonucleotides see Rossi et al., *supra*.

In a preferred application of this invention, the polypeptide encoded by the gene is first identified, so that the

effectiveness of antisense inhibition on translation can be monitored using techniques that include but are not limited to
antibody-mediated tests such as RIAs and ELISA, functional assays, or radiolabeling.

The extended cDNAs of the present invention (or genomic DNAs obtainable therefrom) may also be used in gene therapy approaches based on intracellular triple helix formation. Triple helix oligonucleotides are used to inhibit transcription from a genome. They are particularly useful for studying alterations in cell activity as it is associated with a particular gene. The extended cDNAs (or genomic DNAs obtainable therefrom) of the present invention or, more preferably, a portion of those sequences, can be used to inhibit gene expression in individuals having diseases associated with expression of a particular gene. Similarly, a portion of the extended cDNA (or genomic DNA obtainable therefrom) can be used to study the effect of inhibiting transcription of a particular gene within a cell. Traditionally, homopurine sequences were considered the most useful for triple helix strategies. However, homopyrimidine sequences can also inhibit gene expression. Such homopyrimidine oligonucleotides bind to the major groove at homopurine:homopyrimidine sequences. Thus, both types of sequences from the extended cDNA or from the gene corresponding to the extended cDNA are contemplated within the scope of this invention.

## **EXAMPLE 60**

## Preparation and use of Triple Helix Probes

The sequences of the extended cDNAs (or genomic DNAs obtainable therefrom) are scanned to identify 10-mer to 20-mer homopyrimidine or homopyrime stretches which could be used in triple-helix based strategies for inhibiting gene expression. Following identification of candidate homopyrimidine or homopyrime stretches, their efficiency in inhibiting gene expression is assessed by introducing varying amounts of oligonucleotides containing the candidate sequences into tissue culture cells which normally express the target gene. The oligonucleotides may be prepared on an oligonucleotide synthesizer or they may be purchased commercially from a company specializing in custom oligonucleotide synthesis, such as GENSET, Paris, France.

The oligonucleotides may be introduced into the cells using a variety of methods known to those skilled in the art, including but not limited to calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection or native uptake.

Treated cells are monitored for altered cell function or reduced gene expression using techniques such as Northern blotting, RNase protection assays, or PCR based strategies to monitor the transcription levels of the target gene in cells which have been treated with the oligonucleotide. The cell functions to be monitored are predicted based upon the homologies of the target gene corresponding to the extended cDNA from which the oligonucleotide was derived with known gene sequences that have been associated with a particular function. The cell functions can also be

predicted based on the presence of abnormal physiologies within cells derived from individuals with a particular inherited disease, particularly when the extended cDNA is associated with the disease using techniques described in Example 53.

The oligonucleotides which are effective in inhibiting gene expression in tissue culture cells may then be introduced in vivo using the techniques described above and in Example 59 at a dosage calculated based on the in vitro results, as described in Example 59.

In some embodiments, the natural (beta) anomers of the oligonucleotide units can be replaced with alpha anomers to render the oligonucleotide more resistant to nucleases. Further, an intercalating agent such as ethidium bromide, or the like, can be attached to the 3' end of the alpha oligonucleotide to stabilize the triple helix. For information on the generation of oligonucleotides suitable for triple helix formation see Griffin et al. (Science 245:967-10 971 (1989).

## **EXAMPLE 61**

## Use of Extended cDNAs to Express an Encoded Protein in a Host Organism

The extended cDNAs of the present invention may also be used to express an encoded protein in a host organism to produce a beneficial effect. In such procedures, the encoded protein may be transiently expressed in the host organism or stably expressed in the host organism. The encoded protein may have any of the activities described above. The encoded protein may be a protein which the host organism lacks or, alternatively, the encoded protein may augment the existing levels of the protein in the host organism.

A full length extended cDNA encoding the signal peptide and the mature protein, or an extended cDNA encoding only the mature protein is introduced into the host organism. The extended cDNA may be introduced into the host organism using a variety of techniques known to those of skill in the art. For example, the extended cDNA may be injected into the host organism as naked DNA such that the encoded protein is expressed in the host organism, thereby producing a beneficial effect.

Alternatively, the extended cDNA may be cloned into an expression vector downstream of a promoter which is active in the host organism. The expression vector may be any of the expression vectors designed for use in gene therapy, including viral or retroviral vectors.

The expression vector may be directly introduced into the host organism such that the encoded protein is expressed in the host organism to produce a beneficial effect. In another approach, the expression vector may be introduced into cells in vitro. Cells containing the expression vector are thereafter selected and introduced into the host organism, where they express the encoded protein to produce a beneficial effect.

## EXAMPLE 62

30

## Use Of Signal Peptides Encoded By 5' Ests Or Sequences

#### Obtained Therefrom To Import Proteins Into Cells

The short core hydrophobic region (h) of signal peptides encoded by the 5'ESTS or extended cDNAs derived from the 5'ESTs of the present invention may also be used as a carrier to import a peptide or a protein of interest, so-

called cargo, into tissue culture cells (Lin et al., J. Biol. Chem., 270: 14225-14258 (1995); Du et al., J. Peptide Res., 51: 235-243 (1998); Rojas et al., Nature Biotech., 16: 370-375 (1998)).

When cell permeable peptides of limited size (approximately up to 25 amino acids) are to be translocated across cell membrane, chemical synthesis may be used in order to add the h region to either the C-terminus or the N-terminus to the cargo peptide of interest. Alternatively, when longer peptides or proteins are to be imported into cells, nucleic acids can be genetically engineered, using techniques familiar to those skilled in the art, in order to link the extended cDNA sequence encoding the h region to the 5' or the 3' end of a DNA sequence coding for a cargo polypeptide. Such genetically engineered nucleic acids are then translated either *in vitro* or *in vivo* after transfection into appropriate cells, using conventional techniques to produce the resulting cell permeable polypeptide. Suitable hosts cells are then simply incubated with the cell permeable polypeptide which is then translocated across the membrane.

This method may be applied to study diverse intracellular functions and cellular processes. For instance, it has been used to probe functionally relevant domains of intracellular proteins and to examine protein-protein interactions involved in signal transduction pathways (Lin et al., supra; Lin et al., J. Biol. Chem., 271: 5305-5308 (1996); Rojas et al., J. Biol. Chem., 271: 27456-27461 (1996); Liu et al., Proc. Natl. Acad. Sci. USA, 93: 11819-11824 (1996); Rojas et al., Bioch. Biophys. Res. Commun., 234: 675-680 (1997)).

Such techniques may be used in cellular therapy to import proteins producing therapeutic effects. For instance, cells isolated from a patient may be treated with imported therapeutic proteins and then re-introduced into the host organism.

Alternatively, the h region of signal peptides of the present invention could be used in combination with a nuclear localization signal to deliver nucleic acids into cell nucleus. Such oligonucleotides may be antisense oligonucleotides or oligonucleotides designed to form triple helixes, as described in examples 59 and 60 respectively, in order to inhibit processing and maturation of a target cellular RNA.

## **EXAMPLE 63**

## Reassembling & Resequencing of Clones

Full length cDNA clones obtained by the procedure described in Example 27 were double-sequenced. These sequences were assembled and the resulting consensus sequences were then reanalyzed. Open reading frames were reassigned following essentially the same process as the one described in Example 27.

After this reanalysis process a few abnormalities were revealed. The sequences presented in SEO ID NOs: 47, 73, 79, 89, 91, 96, 126, 128, 134, and 139 are apparently unlikely to be genuine full length cDNAs. These clones are missing a stop codon and are thus more probably 3' truncated cDNA sequences. Similarly, the sequences presented in SEO ID NOs: 45, 50, 54, 57, 73, 74, 89, 92, 95, 98, 126, 129, 130, 131 and 139 may also not be genuine full length cDNAs based on homology studies with existing protein sequences. Although both of these sequences encode a potential start methionine each could represent a 5' truncated cDNA.

In addition, SEQ ID NO: 115 was found to be an alternatively spliced transcript and the identities of some of the bases in SEQ ID NO: 131 were corrected.

Finally, after the reassignment of open reading frames for the clones, new open reading frames were chosen in some instances. For example, in the case of SEO ID NOs: 41, 47, 50, 52, 54-56, 58, 59, 61, 74, 75, 79, 84, 89, 91, 92, 96, 98, 103, 105, 106, 126, 129, 131, and 133 the new open reading frames were no longer predicted to contain a signal peptide.

As discussed above, Table IV provides the sequence identification numbers of the extended cDNAs of the present invention, the locations of the full coding sequences in SEO ID NOs: 40-140 and 242-377 (i.e. the nucleotides encoding both the signal peptide and the mature protein, listed under the heading FCS location in Table IV), the locations of the nucleotides in SEO ID NOs: 40-140 and 242-377 which encode the signal peptides (listed under the heading SigPep Location in Table IV), the locations of the nucleotides in SEO ID NOs: 40-140 and 242-377 which encode the mature proteins generated by cleavage of the signal peptides (listed under the heading Mature Polypeptide Location in Table IV), the locations in SEO ID NOs: 40-140 and 242-377 of stop codons (listed under the heading Stop Codon Location in Table IV) the locations in SEO ID NOs: 40-140 and 242-377 of polyA signals (listed under the heading g PolyA Signal Location in Table IV) and the locations of polyA sites (listed under the heading PolyA Site Location in Table IV).

As discussed above, Table V lists the sequence identification numbers of the polypeptides of SEQ ID NOs: 141-241 and 378-513, the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the full length polypeptide (second column), the locations of the amino acid residues of SEQ ID NOs: 141-241 and 378-513 in the signal peptides (third column), and the locations of the amino acid residues of SEQ ID NOs: 141-241 and 379-513 in the mature polypeptide created by cleaving the signal peptide from the fall length polypeptide (fourth column). In Table V, and in the appended sequence listing, the first amino acid of the mature protein resulting from cleavage of the signal peptide is designated as amino acid number 1 and the first amino acid of the signal peptide is designated with the appropriate negative number, in accordance with the regulations governing sequence listings.

25

## **EXAMPLE 64**

## **Functional Analysis of Predicted Protein Sequences**

Following double-sequencing, new contigs were assembled for each of the extended cDNAs of the present invention and each was compared to known sequences available at the time of filing. These sequences originate from the following databases: Genbank (release 108 and daily releases up to October, 15, 1998), Genseq (release 32) PIR (release 33) and SwissProt (release 35). The predicted proteins of the present invention matching known proteins were further classified into 3 categories depending on the level of homology.

The first category contains proteins of the present invention exhibiting more than 70% identical amino acid residues on the whole length of the matched protein. They are clearly close homologues which most probably have the same function or a very similar function as the matched protein.

The second category contains proteins of the present invention exhibiting more remote homologies (40 to 70% over the whole protein) indicating that the protein of the present inventionmay have functions similar to those of the homologous protein.

The third category contains proteins exhibiting homology (90 to 100%) to a domain of a known protein indicating that the matched protein and the protein of the invention may share similar features.

It should be noted that the numbering of amino acids in the protein sequences discussed in Figures 10 to 15, and Table VIII, the first methionine encountered is designated as amino acid number 1. In the appended sequence listing, the first amino acid of the mature protein resulting from cleavage of the signal peptide is designated as amino acid number 1, and the first amino acid of the signal peptide is designated with the appropriate negative number, in accordance with the regulations governing sequence listings.

In addition all of the corrected amino acid sequences (SEO ED NOs: 141-241 and 378-513) were scanned for the presence of known protein signatures and motifs. This search was performed against the Prosite 15.0 database, using the Proscan software from the GCG package. Functional signatures and their locations are indicated in Table VIII.

## 15 A) Proteins which are closely related to known proteins

## Protein of SEO ID NO: 217

The protein of SEQ ID NO: 217 encoded by the extended cDNA SEQ ID NO: 116 isolated from lymphocyte shows complete identity to a human protein TFAR19 that may play a role in apoptosis (Genbank accession number AF014955, SEQ ID NO: 516) as shown by the alignment in figure 10.

Taken together, these data suggest that the protein of SEQ ID NO: 217 may be involved in the control of development and homeostasis. Thus, this protein may be useful in diagnosis and/or treating several types of disorders including, but not limited to, cancer, autoimmune disorders, viral infections such as AIDS, neurodegenerative disorders, osteoporosis.

## 25 Proteins of SEQ ID NOs: 174, 175 and 232

The proteins of SEQ ID NOs: 174, 175 and 232 encoded by the extended cDNAs SEQ ID NOs:. 73, 74 and 131 respectively and isolated from lymphocytes shows complete extensive homologies to a human secreted protein (Genseq accession number W36955, SEQ ID NO: 517). As shown by the alignments of figure 11, the amino acid residues are identical to those of the 110 amino acid long matched protein except for positions 51 and 108-110 of the matched protein for the protein of SEQ ID NOs: 174, for positions 48, 94 and 108-110 of the matched protein of SEQ ID NOs:175 and for positions 94, and 108-110 of the matched protein for the protein of SEQ ID NOs: 232. Proteins of SEQ ID NOs: 174 and 232 may represent alternative forms issued from alternative use of polyadenylation signals.

Taken together, these data suggest that the proteins of SEO ID NOs: 174, 175 and 232 may play a role in cell proliferation and/or differentiation, in immune responses and/or in haematopoeisis. Thus, this protein or part therein,

may be useful in diagnosing and treating several disorders including, but not limited to, cancer, immunological, haematological and/or inflammatory disorders. It may also be useful in modulating the immune and inflammatory responses to infectious agents and/or to suppress graft rejection.

## 5 Proteins of SEQ ID NO: 231

The protein of SEQ ID NO: 231 encoded by the extended cDNA SEQ ID NO: 130 shows extensive homology with the human E25 protein (Genbank accession number AF038953, SEQ ID NO: 515). As shown by the alignments in figure 12, the amino acid residues are identical except for position 159 in the 263 amino acid long matched sequence. The matched protein might be involved in the development and differentiation of haematopoietic stem/progenitor cells.

10 In addition, it is the human homologue of a murine protein thought to be involved in chondro-osteogenic differentiation and belonging to a novel multigene family of integral membrane proteins (Deleersnijder et al, J. Biol. Chem., 271: 19475-19482 (1996)).

The protein of invention contains two short segments from positions 1 to 21 and from 100 to 120 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10:685-686 (1994)). The first transmembrane domains matches exactly those predicted for the murine E25 protein.

Taken together, these data suggest that the protein of SEQ ID NO: 231 may be involved in cellular proliferation and differentiation. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer and embryogenesis disorders.

#### 20 Protein of SEQ ID NO: 196

The protein of SEQ ID NO: 196 encoded by the extended cDNA SEQ ID NO: 95 shows extensive homology with the human seventransmembrane protein (Genbank accession number Y11395, SEQ ID NO: 518) and its murine homologue (Genbank accession number Y11550). As shown by the alignments in figure 13, the amino acid residues are identical except for position 174 in the 399 amino acid long human matched sequence. The matched protein potentially associated to stomatin may act as a G-protein coupled receptor and is likely to be important for the signal transduction in neurons and haematopoietic cells (Mayer et al, Biochem. Biophys. Acta., 1395: 301-308 (1998)).

Taken together, these data suggest that the protein of SEQ ID NOs: 196 may be involved in signal transduction. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases cardiovascular disorders, hypertension, renal injury and repair and septic shock.

#### Protein of SEQ ID NO: 158

The protein of SEQ ID NOs: 158 encoded by the extended cDNA SEQ ID NO: 57 shows homology with the murine subunit 7a of the COP9 complex (Genbank accession number AF071316, SEQ ID NO: 520). As shown by the

alignments in figure 14, the amino acid residues are identical except for positions 90, 172 and 247 in the 275 amino acid long matched sequence. This complex is highly conserved between mammals and higher plants where it has been shown to act as a repressor of photomorphogenesis All the components of the mammalian COP9 complex contain structural features also present in components of the proteasome regulatory complex and the translation initiation complex eIF3 complex, suggesting that the mammalian COP9 complex is an important cellular regulator modulating multiple signaling pathways (Wei et al, Curr. Biol., 8: 919-922 (1998)).

Taken together, these data suggest that the protein of SEQ ID NO: 158 may be involved in cellular signaling, probably as a subunit of the human COP9 complex. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, cardiovascular disorders, hypertension, renal injury and repair and septic shock.

## Protein of SEQ ID NO: 226

The protein of SEQ ID NO: 226 encoded by the extended cDNA SEQ ID NO: 125 shows homology with the bovine subunit B14.5B of the NADH-ubiquinone oxidureductase complex (Arizmendi et al, FEBS Lett., 313: 80-84 (1992) and Swissprot accession -number Q02827, SEQ ID NO: 514). As shown by the alignments in figure 15, the amino acid residues are identical except for positions 3-4, 6-12, 32-34, 47, 53-55, 67 and 69-74 in the 120 amino acid long matched sequence. This complex is the first of four complexes located in the inner mitochondrial membrane and composing the mitochondrial electron transport chain. Complex I is involved in the dehydrogenation of NADH and the transportation of electrons to coenzyme Q. It is composed of 7 subunits encoded by the mitochondrial genome and 34 subunits encoded by the nuclear genome. It is also thought to play a role in the regulation of apoptosis and necrosis. Mitochondriocytopathies due to complex I deficiency are frequently encountered and affect tissues with a high energy demand such as brain (mental retardation, convulsions, movement disorders), heart (cardiomyopathy, conduction disorders), kidney (Fanconi syndrome), skeletal muscle (exercise intolerance, muscle weakness, hypotonia) and/or eye (opthmaloplegia, ptosis, cataract and retinopathy). For a review on complex I see Smeitink et al., Hum. Mol. Gent., 7: 1573-1579 (1998).

Taken together, these data suggest that the protein of SEQ ID NO: 226 may be part of the mitochondrial energy-generating system, probably as a subunit of the NADH-ubiquinone oxidoreductase complex. Thus, this protein or part therein, may be useful in diagnosing and/or treating several disorders including, but not limited to, brain disorders (mental retardation, convulsions, movement disorders), 'heart disorders (cardiomyopathy, conduction disorders), kidney disorders (Fanconi syndrome), skeletal muscle disorders (exercise intolerance, muscle weakness, hypotonia) and/or eye disorders opthmalmoplegia, ptosis, cataract and retinopathy).

B) Proteins which are remotely related to proteins with known functions Proteins of SEO ID NOs: 149, 150 and 211 The proteins of SEO ID NOs: 1.49,150 and 211 encoded by the extended cDNAs SEO ID NOs: 48, 49 and 110 respectively and found in, skeletal muscle shows homologies with T1/ST2 ligand polypeptide of either human (Genbank accession number U41804 and Genseq accession number W09639) or rodent species (Genbank accession number U41805 and Genseq accession number W09640). These polypeptides are thought to be cytokines that bind to the ST2 receptor, a member of the immunoglobulin family homologous to the interleukin-1 receptor and present on some lymphoma cells. They are predicted to be cell-surface proteins containing a short transmembrane domain. (Gayle et al, J. Biol. Chem., 271: 5784-5789 (1996)). Proteins of SEO ID NOs: 149, 150 and 211 may represent alternative forms issued from alternative use of polyadenylation signals.

The protein of invention contains two short transmembrane segments from positions 5 to 25 and from 195 to 20 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10:685-686 (1994)). The second transmembrane domain matches exactly those of the matched cell-surface protein.

Taken together, these data suggest that the protein of SEQ ID NOs: 149, 150 and 211 may act as a cytokine, thus may play a role in the regulation of cell growth and differentiation and/or in the regulation of the immune response. Thus, this protein or part therein, may be useful in diagnosing and treating several disorders including, but not limited to, cancer, immunological, haematological and/or inflammatory disorders. It may also be useful in modulating the immune and inflammatory responses to infectious agents such as HIV and/or to suppress graft rejection.

#### Protein of SEQ ID NO: 177

The protein SEQ ID NO: 177 found in testis encoded by the extended cDNA SEQ ID NO: 76 shows homologies to serine protease inhibitor proteins belonging to the pancreatic trypsin inhibitor family (Kunitz) such as the extracellular proteinase inhibitor named chelonianin (Swissprot accession number P00993). The characteristic PROSITE signature of this family is conserved in the protein of the invention (positions 69 to 87) except for a drastic change of the last cysteine residue into an arginine residue.

Taken together, these data suggest that the protein of SEQ ID NO: 177 may be a protease inhibitor, probably of the Kunitz family. Thus, this protein or part therein, may be useful in diagnosing and treating several disorders including but not limited to, cancer and neurodegenerative disorders such as Alzheimer's disease.

## Protein of SEQ ID NO: 146

The protein SEQ ID NO: 146 encoded by the extended cDNA SEQ ID NO: 45 shows homology to human apolipoprotein L (Genbank accession number AFO19225). The matched protein is a secreted high density lipoprotein associated with apoA-l-containing lipoproteins which play a key role in reverse cholesterol transport.

Taken together, these data suggest that the protein of SEQ ID NO. 146 may play a role in lipid metabolism.

Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to.

hyperlipidemia, hypercholesterolemia, atherosclerosis, cardiovascular disorders such as, coronary heart disease, and neurodegenerative disorders such as Alzheimer's disease or dementia.

## Protein of SEQ ID NO: 163

5

The protein SEQ ED NO: 163 encoded by the extended cDNA SEQ ID NO: 62 shows homology to the yeast autophagocytosis protein AUT1 (SwissProt accession number P40344). The matched protein is required for starvation-induced non-specific bulk transport of cytoplasmic proteins to the vacuole.

Taken together, these data suggest that the protein of SEQ ID NO: 163 may play a role in protein transport.

Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to,
autoimmune disorders and immune disorders due to dysfunction of antigen presentation.

## C) Proteins homologous to a domain of a protein with known function

## Protein of SEO ID NO: 214

The protein of SEQ ID NO: 214 encoded by the extended cDNA SEQ ID NO: 113 and expressed in adult brain shows extensive homology to part of the murine SHYC protein (Genbank accession number AF072697) which is expressed in the developing and embryonic nervous system as well as along the olfactory pathway in adult brains (Köster et al., Neuroscience Letters., 252: 69-71 (1998)).

Taken together, these data suggest that the protein of SEQ ID NO: 214 may play a role in nervous system development and function. Thus, this protein may be useful in diagnosing and/or treating cancer and/or brain disorders, including neurodegenerative disorders such as Alzheimer's and Parkinson's diseases.

## Protein of SEQ ID NO: 225

The protein of SEO ID NO: 225 encoded by the extended cDNA SEO ID NO: 124 and expressed in adult prostate belong to the phosphatidylethanolainin-binding protein from which it exhibits the characteristic PROSITE signature from positions 90 to 112 (see table VIII). Proteins from this widespread family, from nematodes to fly, yeast, rodent and primate species, bind hydrophobic ligands such as phospholipids and nucleotides. They are mostly expressed in brain and in testis and are thought to play a role in cell growth and/or maturation, in regulation of the sperm maturation, motility and 'in membrane remodeling. They may act either through signal transduction or through oxidoreduction reactions (for a review see Schoentgen and Jollès, *FEBS Letters*, 369 : 22-26 (1995)).

Taken together, these data suggest that the protein of SEQ ID NO: 225 may play a role in cell. Thus, these growth, maturation and in membrane remodeling and/or may be related to male fertility. Thus, this protein may be useful in diagnosing and/or treating cancer, neurodegenerative diseases, and/of, disorders related to male fertility and sterility.

#### Protein of SEO ID NO: 153

The protein of SEQ ID NO: 153 encoded by the extended cDNA SEQ ID NO. 52 and expressed in brain exhibits homology to different integral membrane proteins. These membrane proteins include the nematode protein SRE-2 (Swissprot accession number Q09273) that belongs to the multigene SRE family of *C. elegans* receptor-like proteins and a family of tricarboxylate carriers conserved between flies and mammals. One member of this matched family is the rat tricarboxylate carrier (Genbank accession number S70011), an anion transporter localized in the inner membrane of mitochondria and involved in the biosynthesis of fatty acids and cholesterol. The protein of the invention contains a short transmembrane segments from positions 5 to 25 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10:685-686 (1994)).

Taken together, these data suggest that the protein of SEQ ID NO: 153 may play a role in signal transduction and/or in molecule transport. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, immune disorders, cardiovascular disorders, hypertension, renal injury and repair and septic shock

#### Protein of SEQ ID NO: 213

15

The protein of SEQ ID NO: 213 encoded by the extended cDNA SEQ ID NO: 112 and expressed in brain exhibits homology with part of the tRNA pseudouridine 55 synthase found in *Escherichia Coli* (Swissprot accession number P09171). This bacterial protein belongs to the NAP57/CBF5/TRUB family of nucleolar proteins found in bacteria, yeasts and mammals involved in rRNA or tRNA biosynthesis, ribosomal subunit assembly and/or centromere/mircotubule binding.

Taken together, these data suggest that the protein of SEQ ID NO: 213 may play a role in rRNA or tRNA biogensis and function. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, hearing loss or disorders linked to chromosomal instability such as dyskeratosis.

## Protein of SEQ ED NO: 240

The protein of SEQ ID NO: 240 encoded by the extended cDNA SEQ ID NO: 139 and expressed in brain exhibits homology with a family of eukaryotic cell surface antigens containing 4 transmembrane domains. The PROSITE signature for this family is conserved in the protein of the invention except for a substitution of an alanine residue in place of any of the following hydrophic residues: leucine, valine, isoleucine or methionine (positions 21 to 36).

The protein of the invention contains three short transmembrane segments from positions 6 to 26, 32 to 52 and from 56 to 76 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10: 685-686 (1994)). These transmembrane domains match the last three transmembrane domains of the matched protein family.

Taken together, these data suggest that the protein of SEQ ID NO: 240 may play a role in immunological and/or inflammatory responses, probably as a cell surface antigen. Thus, this protein or part therein, may be useful in diagnosing and treating several disorders including, but not limited to, cancer, immunological, haematological and/or

inflammatory disorders. It may also be useful in modulating the immune and inflammatory responses to infectious agents and/or to suppress graft rejection.

## Protein of SEO ID NO: 239

5

10

The protein of SEQ ID NO: 239 encoded by the extended cDNA SEQ ID NO: 138 exhibits homology with a conserved region in a family of NA+/H+ exchanger conserved in yeast, nematode and mammals. These cation/proton exchangers are integral membrane proteins with 5 transmembrane segments involved in intracellular pH regulation, maintenance of cell volume, reabsorption of sodium across specialized epithelia, vectorial transport and are also thought to play a role in signal transduction and especially in the induction of cell proliferation and in the induction of apoptosis.

The protein of invention contains four short transmembrane segments from positions 21 to 41, 48 to 68 and from 131 to 151 as predicted by the software TopPred II (Claros and von Heijne, *CABIOS applic. Notes*, 10:685-686 (1994)). The third and fourth transmembrane domains match the fourth and fifth transmembrane segments of the matched family of proteins.

Taken together, these data suggest that the protein of SEO ID NO: 239 may play a role in membrane permeability and/or in signal transduction. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, cardiovascular disorders, hypertension, renal injury and repair, septic shock as well as disorders of membrane permeability such as diarrhea.

## Protein of SEQ ID NO: 200

The protein of SEQ ID NO: 200 encoded by the extended cDNA SEQ ED NO: 99 and expressed in brain exhibits extensive homology to the N-terminus of cell division cycle protein 23 (Genbank accession number AF053977) and also to a lesser extent to its homologue in Saccharomyces cerevisiae. The matched protein is required for chromosome segregation and is part of the anaphae-promoting complex necessary for cell cycle progression to mitosis.

Taken together, these data suggest that the protein of SEQ ID NO: 200 may play a role in cellular mitosis.

Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer and leukemia.

## Protein of SEQ ID NO: 230

The protein of SEQ ID NO: 230 encoded by the extended cDNA SEQ ID NO: 129 exhibits extensive homology to

the C-terminus of the eta subunit of T-complex polypeptide 1 conserved from yeasts to mammals, and even complete identity with the last 54 amino acid residues of the human protein (Genbank accession number AFO26292). The matched protein is a chaperonin which assists the folding of actins and tubulins in eukaryotic cells upon ATP hydrolysis.

Taken together, these data suggest that the protein of SEQ ID NO: 230 may play a role in the folding, transport, assembly and degradation of proteins. Thus, this protein may be useful in diagnosing and/or treating several

types of disorders including, but not limited to, cancer, cardiovascular disorders, immune disorders, neurodegenerative disorders, osteoporosis and arthritis.

## Protein of SEQ ED NO: 167

5

The protein of SEQ ID NO: 167 encoded by the extended cDNA SEQ ID NO: 66 exhibits homology to a monkey pepsinogen A-4 precursor (Swissprot accession number P27678) and to related members of the aspartyl protease family. The matched protein belongs to a family of widely distributed proteolytic enzymes known to exist in vertebrate, fungi, plants, retroviruses and some plant viruses.

Taken together, these data suggest that the protein of SEQ ID NO: 167 may play a role in the degradation of proteins. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, autoimmune disorders and immune disorders due to dysfunction of antigen presentation.

#### Protein of SEO ID NO: 179

The protein of SEQ ID NO: 179 encoded by the extended cDNA SEQ ID NO: 78 found in testis exhibits homology to part of mammalian colipase precursors. Colipases are secreted cofactors for pancreatic lipases that allow the lipase to anchor at the water-lipid interface. Colipase plays a crucial role in the intestinal digestion and absorption of dietary fats. The 5 cysteines characteristic for this protein family are conserved in the protein of the invention although the colipase PROSITE signature is not.

Taken together, these data suggest that the protein of SEQ ED NO: 179 may play a role in the lipid metabolism and/or in male fertility. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, hyperlipidemia, hypercholesterolemia, atherosclerosis, cardiovascular disorders such as coronary heart disease, and neurodegenerative disorders such as Alzheimer's disease or dementia, and disorders linked to male fertility.

## 25 Protein of SEQ ID NO: 227

The protein of SEO ID NO: 227 encoded by the extended cDNA SEO ID NO: 126 exhibits extensive homology to the ATP binding region of a whole family of serine/threonine protein kinases belonging to the CDC2/CDC28 subfamily. The PROSITE signature characteristic for this domain is present in the protein of the invention from positions 10 to 34.

Taken together, these data suggest that the protein of SEQ ED NO: 158 may bind ATP, and even be a protein 30 kinase. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, neurodegenerative diseases, cardiovascular disorders, hypertension, renal injury and repair and septic shock.

Although this invention has been described in terms of certain preferred embodiments, other embodiments which will be apparent to those of ordinary skill in the art in view of the disclosure herein are also within the scope of this invention. Accordingly, the scope of the invention is intended to be defined only by reference to the appended claims.

As discussed above, the extended cDNAs of the present invention or portions thereof can be used for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern . gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to 10 compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination for expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins or polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other 25 protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing 30 such methods include without limitation "Molecular Cloning; A Laboratory Manual", 2d ed., Cole Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology; Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a

nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

## SEQUENCE LISTING FREE TEXT

The following free text appears in the accompanying Sequence Listing: In vitro transcription product oligonucleotide

5 promoter
transcription start site
Von Heijne matrix
Score
matinspector prediction

10 name

**TABLE I** 

SEQ ID NO. in Present application	Provisional Application Disclosing Sequence	SEQ ID NO. in provisional application
40	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	51
41	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	72
42	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	52
. 43	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	78
- 44	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	73
45	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	41
46	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	67
47	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	82
48	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	80
49	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	81
50	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	53
51	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	54
52	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	195
53	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	44
54	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	46
55	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	68
56	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	48
57	U.S. Provisional Patent Application Serial No. 60/096, 116, filed Aug. 10, 1998	55
58	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	49
59	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	50
60	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	97
61	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	51
62	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	69
63	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	49
64	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	199
65	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	53
66	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	57
67	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	54
68	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	55
69	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	58
70	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	59

CONT. TABLE I		٠.
71 .	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	60
72	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	112
73	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	52
74	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	59
75	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	60
76	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	. 136
77	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	75
78	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	61
79	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	61
80	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	130
81	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	65
82	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	54
83	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	78
84	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	63
85	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	65
86	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	152
87	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	66
88	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	67
89	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	60
90	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	68
91	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	61
92	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	62
93	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	166
94	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	70
95	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	73
96	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	63
97	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	52
98	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	62
99	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	176
100	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998,	63
101	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	187
102	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	190
103	U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	83
104	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	180
105	U.S. Provisional Patent Application Serial No. 60/096,116, filed Aug. 10, 1998	64
106	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	69

-102-	
···	٠.
U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	40
U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	77
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	43
U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	82
U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998	76
U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	43
U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	46
U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	47
U.S. Provisional Patent Application Serial No. 60/066,677, filed Nov. 13, 1997	53
U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998	58
	74
	71
	145
	67
	58
	72
l:	73
	70
	40
	44
	45
	47 .
	48
	51
	50
	56
	57
	71
	72
	64
	65
	66
	74
	67
	75
U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	76
	U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998  U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998  U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998  U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998  U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998  U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998  U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998  U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998  U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998  U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998  U.S. Provisional Patent Application Serial No. 60/074,121, filed Feb. 9, 1998  U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998  U.S. Provisional Patent Application Serial No. 60/081,563, filed Apr. 13, 1998  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089,957, filed Dec. 17, 1997  U.S. Provisional Patent Application Serial No. 60/089

CUNI. TABLE I		
244	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	77
245	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	78
246	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	79
247	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	80
248	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	81
249	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	. 82
250	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	83
251	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	84
252	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	85
253	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	86
254	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	87
255	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	88
256	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	89
257	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	90
258	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	91
259	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	92
260	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	93
261	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	94
262	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	95
263	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	96
264	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	97
265	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	98
266	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	99
267	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	100
268	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	101
269	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	102
270	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	103
271	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	104
272	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	105
273	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	106
274	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	107
275	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	108
276	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	109
277	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	110
278	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	111
279	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	112
	.,	112

<u>C</u>	ONT. TABLE I		·.
	280	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	113
	281	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	114
	282	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	115
	283	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	116
	284	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	117
	285	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	118
	286	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	119
	287	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	120
	288	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	121
	289	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	122
	290	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	123
	291	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	124
	292	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	125
	293	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	126
	294	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	127
	295	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	128
	296	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	129
	297	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	130
	298	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	131
	299	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	132
	300	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	133
	301	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	134
	302	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	135
	303	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	136
	304	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	137
	305	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	138
	306	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	139
	307	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	140
	308	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	141
	309	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	142
	310	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	143
	311	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	144
	312	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	145
	313	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	146
	314	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	147
	315	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	148

CONT. TABLE I		٠.
316	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	149
317	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	150
318	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	151
319	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	152
320	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	153
321	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	154
322	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	155
323	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	156
324	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	157
325	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	158
326	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	159
327	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	160
328	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	161
329	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	162
330	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	163
331	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	164
332	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	165
333	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	166
334	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	167
335	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	168
336	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	169
337	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	170
338	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	171
339	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	172
340	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	173
341	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	174
342	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	175
343	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	176
344	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	177
345	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	178
346	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	179
347	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	180
348	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	181
349	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	182
350	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	183
351	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	184

GOINT. TABLE I		··
352	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	185
353	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	186
354	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	187
355	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	188
356	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	189
357	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	190
358	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	191
359	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	192
360	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	193
361	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	194
362	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	195
363	L.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	196
364	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	197
365	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	1998
366	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	199
367	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	200
368	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	201
369	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	202
370	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	203
371	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	204
372	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	205
373	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	206
374	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	207
375	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	208
376	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	209
377	U.S. Provisional Patent Application Serial No. 60/069,957, filed Dec. 17, 1997	210

TABLE II : Parameters used for each step of EST analysis

	,	Search Charac	teristics	Selection Characteristics	
Step	Program	Strand	Parameters	Identity (%))	Length (bp)
Miscellaneous	Blastn	both	S-61 X-16	90	17
tRNA	Fasta	both		. 80	60
rRNA	Blastn	both	S=108	80	40
mtRNA	Blastn	both ·	S=108	80	40
Procaryotic	Blastn	both	S-144	90	40
Fungal	Blastn	both '	S=144	90	40
Alu	fasta*	both		70	40
L1 .	Blastn	both	S-72	70	40
Repeats	Blastn	both	S-72	70	40
Promoters	Blastn	top	S-54 X-16	90	15⊥
Vertebrate	fasta*	both	S=108	90	30
ESTs '	Blatsn	both	S-108 X-16	90	30
Proteins	blastxŋ	top	E-0.001		

<sup>•</sup> use "Quick Fast" Database Scanner

 $oldsymbol{\perp}$  alignment further constrained to begin closer than 10bp to EST\5' end

<sup>5</sup> η using BLOSUM62 substitution matrix

TABLE III: Parameters used for each step of extended cDNA analysis

	Search characte	ristics	Selection characteristics			:s
Step	Program	Strand	Parameters	Identity (%)	Length (bp)	Comments
miscellaneous •	FASTA	both	·	90	15	
tRNA <sup>4</sup>	FASTA	both	1.	80	90	
rRNA*	BLASTN	both.	S-108	80	40	
mtRNA*	BLASTN	both	S-108	80	40	
Procaryotic <sup>1</sup>	BLASTN	both	S-144	90	40	
Fungal*	BLASTN	both	S-144	90	40	
Alu*	BLASTN	both	S-72	70	40	max 5 matches, masking
111	BLASTN	both	S-72	70	40	max 5 matches, masking
Repeats*	BLASTN	both	S-72	70	40	masking
PolyA	BLAST2N	top	W-6,S-10,E-1000	90	8	in the last 20 nucleotides
Polyadenylati on signal		top	AATAAA allowing 1 mis	match	•	in the 50 nucleotides preceding the 5' end of the polA
Vertebrate*	BLASTN then FASTA	both		90 then 70	30	first BLASTN and then FASTA on matching sequences
ESTs*	BLAST2N	both		90	30	
Geneseq	BLASTN	both	W-8, B-10	90	30	
ORF	BLASTP	top	W-8, B-10			on ORF proteins, max 10 matches
Proteins*	BLASTX	top	E-0.001	70	30	

 <sup>\*</sup> steps common to EST analysis and using the same algorithms and parameters
 \* steps also used in EST analysis but with different algorithms and/or parameters

TABLE IV

			IAL	BLE IV		
ld	FCS Location	SigPep Location	Mature Polypeptide Location	Stop Codon Location	PolyA Signal Location	PolyA Site Location
40	7 through 471	7 through 99	100 through 471		537 through 542	554 through 568
41	168 through 332	·	168 through 332	333	557 through 562	
42	51 through 251	'51 through 110	111 through 251	252	849 through 854	882 through 895
43	20 through 613	20 through 82	83 through 613	614	· ·	002 through 033
44	12 through 416	12 through 86	87 through 416	417	425 through 430	445 through 458
45	276 through 1040	276 through 485	486 through 1040	1041		2024 through 2036
46	443 through 619	443 through 589	590 through 619	620	1.	1267 through 1276
47	206 through 747		206 through 747	<del>                                     </del>	1.	1207 titrough 1276
48	36 through 521	. 36 through 104	105 through 521	522	528 through 533	548 through 561
49	36 through 395	36 through 1D4	105 through 395	396	599 through 604	
50	21 through 41	1.	21 through 41	42	328 through 333	619 through 632
51	35 through 631	35 through 160	161 through 631	632	901 through 906	357 through 370
52	271 through 399		271 through 399	400	· ·	979 through 994
53	103 through 252	103 through 213	214 through 252	253		. 500 ab 507
54	2 through 460		2 through 460	461	713 through 718	588 through 597
55	31 through 231	-	31 through 231	232	769 through 774	735 through 748
56	305 through 565	<del> </del>	305 through 565	566	694 through 699	690 through 703
57	124 through 873	124 through 378	379 through 873	874	1673 through 1678	713 through 725
58	135 through 206	1.	135 through 206	207	850 through 855	1694 through 1705
59	135 through 818	ļ	135 through 818	819	909 through 914	1056 through 1069
60	33 through 290	33 through 92	93 through 290	291	- Cos tineugh 514	1071 through 1084
61	485 through 616	1.	485 through 616	617		
62	54 through 995	54 through 227	228 through 995	996	1130 through 1135	669 through 682
63	657 through 923	657 through 896	897 through 923	924	957 through 962	1181 through 1191
64	18 through 311	18 through 62	63 through 311	312	957 till dugh 962	974 through 1008
65	151 through 426	151 through 258	259 through 426	427	EOE about 510	
66	10 through 1062	10 through 57	58 through 1062	1063	505 through 510	527 through 538
67	78 through 491	78 through 218	219 through 491	492	1710 through 1715	1735 through 1747
68	69 through 371	69 through 287	288 through 371	372	1652 through 1657	1673 through 1686
39	2 through 757	2 through 205	206 through 757	758	510 through 515	530 through 542
70	2 through 1051	2 through 205	206 through 1051	1052		1160 through 1174
71	2 through 1171	2 through 205	206 through 1171	1172	1248 through 1253	1272 through 1285
72	42 through 611	42 through 287	288 through 611	612	1368 through 1373	1386 through 1398
3	62 through 916	62 through 757	758 through 916		787 through 792	808 through 821
4	62 through 520		62 through 520			904 through 916
5	21 through 167	-	21 through 167	521	1124 through 1129	1141 through 1153
6	22 through 318	22 through 93	94 through 318	168	407 -1	·
7	8 through 292	8 through 118	119 through 292	319	497 through 502	516 through 526
8	16 through 378	16 through 84	85 through 378	293	317 through 322	339 through 352
1		. T sundayii 04	oo tiirougii 376	379	502 through 507	522 through 542

CONT TARIFIV

CONT	. TABLE IV					
79	57 through 233	•	57 through 233	•	•	•
80	83 through 340	83 through 124	125 through 340	341	.573 through 578	607 through 660
81	47 through 541	47 through 220	221 through 541	542	•	597 through 605
82	46 through 285	46 through 150	151 through 285	286	364 through 369	385 through 396
83	22 through 240	22 through 84	85 through 240	241	397 through 402	421 through 432
84	89 through 382		89 through 382	383	•	408 through 420
85	80 through 415	80 through 142	143 through 415	416	471 through 476	488 through 501
86	152 through 361	152 through 283	284 through 361	362	-	•
87	32 through 307	32 through 70	71 through 307	308	1240 through 1245	1261 through 1272
88	114 through 734	114 through 239	240 through 734	735	768 through 773	793 through 804
89	199 through 802	•	199 through 802	•	780 through 785	791 through 802
90	38 through 1174	38 through 148	149 through 1174	1175	1452 through 1457	1478 through 1490
91	26 through 361	•	26 through 361	•	•	350 through 361
92	3 through 131	•	3 through 131	132	·	591 through 605
93	33 through 185	33 through 80	81 through 185	186	570 through 575	586 through 591
94	184 through 915	184 through 237	238 through 915	916	1119 through 1124	1139 through 1150
95	58 through 1116	58 through 159	160 through 1116	1117	1486 through 1491	1504 through 1513
96	327 through 417	•	327 through 417	٠	•	404 through 417
97	63 through 398	63 through 206	207 through 398	399	•	•
98	2 through 163	-	2 through 163	164	488 through 493	511 through 522
99	13 through 465	13 through 75	76 through 465	466	·	·
100	20 through 703	20 through 94	95 through 703	704	1000 through 1005	1023 through 1041
101	103 through 294	103 through 243	244 through 294	295	·	·
102	81 through 518	81 through 173	174 through 518	519	·	•
103	66 through 326		66 through 326	327	1066 through 1071	1087 through 1098
104	170 through 289	170 through 250	251 through 289	290	•	• ,,
105	36 through 497		36 through 497	498	650 through 655	663 through 685
106	18 through 320		18 through 320	321	539 through 544	542 through 554
107	71 through 1438	71 through 136	137 through 1438	1439	1644 through 1649	1665 through 1678
108	25 through 318	25 through 75	76 through 318	319	452 through 457	482 through 494
109	84 through 332	84 through 170	171 through 332	333	·	702 through 714
110	32 through 718	32 through 100	101 through 718	719	770 through 775	793 through 805
111	26 through 481	26 through 88	89 through 481	482	755 through 760	775 through 787
112	26 through 562	26 through 187	188 through 562	563		·
113	4 through 810	4 through 279	280 through 810	811	858 through 863	881 through 893
114	55 through 459	55 through 120	121 through 459	460	1444 through 1449	1462 through 1475
115	48 through 248	48 through 161	162 through 248	249	283 through 288	308 through 321
116	25 through 399	25 through 186	187 through 399	400	•	·
117	10 through 1137	10 through 72	73 through 1137	1138	1144 through 1149	1162 through 1173
118	72 through 704	72 through 161	162 through 704	705	772 through 777	·
119	44 through 505	44 through 223	224 through 505	506	·	·
120	25 through 393	25 through 150	151 through 393	394	734 through 739	757 through 770

### CONT. TABLE IV

	IT. TABLE IV			*		
121	58 through 1095	58 through 114	115 through 1095	1096	Ţ	1202 through 1213
122	31 through 660	31 through 90	91 through 660	661	1288 through 1293	1307 through 1318
123	31 through 582	31 through 90	91 through 582	583	816 through 821	840 through 853
124	15 through 695	15 through 80	81 through 695	696	795 through 800	814 through 826
125	74 through 295	. 74 through 196	197 through 295	296	545 through 550	561 through 571
126	440 through 659		440 through 659		601 through 606	
127	38 through 283	38 through 85	86 through 283	284	257 through 262	
128	121 through 477	121 through 288	289 through 477	1	1.	<del> </del>
129	2 through 163		2 through 163	164	292 through 297	310 through 323
130	46 through 675	46 through 87	88 through 675	676	1364 through 1369	1383 through 1392
131	62.through 385		62 through 385	386	974 through 979	987 through 999
132	422 through 550	422 through 475	476 through 550	551		714 through 725
133	124 through 231	•	124 through 231	232		387 through 400
134	131 through 1053	131 through 169	170 through 1053	· .	1019 through 1024	
135	86 through 403	86 through 181	182 through 403	404	1097 through 1102	1117 through 1128
136	37 through 162	37 through 93	94 through 162	163	224 through 229 .	243 through 254
137	31 through 381	31 through 90	91 through 381	382		875 through 886
138	46 through 579	46 through 156	157 through 579	580	•	1.
139	92 through 471	,92 through 172	173 through 471		454 through 459	458 through 471
140	154 through 675	154 through 498	499 through 675	676	819 through 824	838 through 849
242	18 through 173	18 through 77	78 through 173	174	864 through 869	882 through 893
243	17 through 595	17 through 85	86 through 595	596	820 through 825	840 through 851
244	89 through 334	89 through 130	131 through 334	335	462 through 467	484 through 495
245	21 through 614	21 through 83	84 through 614	615	849 through 854	873 through 884
246	94 through 573	94 through 258	259 through 573	574	862 through 867	886 through 897
247	74 through 397	74 through 127	128 through 397	398	472 through 477	507 through 518
248	51 through 242	51 through 116	117 through 242	243	319 through 324	339 through 350
249	111 through 191	111 through 155	156 through 191	192	965 through 970	986 through 996
250	45 through 602	45 through 107	108 through 602	603	828 through 833	850 through 860
251	24 through 560	24 through 101	102 through 560	561	563 through 568	583 through 593
252	109 through 558	109 through 273	274 through 558	559	·	1104 through 1114
253	128 through 835	128 through 220	221 through 835	836	1145 through 1150	1170 through 1181
254	59 through 505	59 through 358	359 through 505	506	1042 through 1047	1062 through 1073
255	1 through 207	1 through 147	148 through 207	208	784 through 789	807 through 818
256	12 through 734	12 through 101	102 through 734	.735	914 through 919	961 through 971
257	378 through 518	378 through 467	468 through 518	519	607 through 612	628 through 640
258	110 through 304	110 through 193	194 through 304	305	708 through 713	732 through 743
259	201 through 419	201 through 272	273 through 419	420	601 through 606	627 through 637
260	123 through 302	123 through 176	177 through 302	303	1279 through 1284	1301 through 1312
261	98 through 673	98 through 376	377 through 673	674		1025 through 1035
262	17 through 463	17 through 232	233 through 463	464	657 through 662	684 through 696
263	263 through 481	263 through 322	323 through 481	482	·	858 through 868

2564         42 through 289         42 through 289         300	CON	T. TABLE IV					
266         279 through 473         279 through 392         363 through 644         474         944 through 849         970 through 891           267         12 through 644         12 through 92         93 through 649         645         1002 through 107         1020 through 1031           268         91 through 459         91 through 174         148 through 327         328         1741 through 1746         1763 through 867           270         12 through 497         12 through 104         105 through 327         328         1741 through 1746         1763 through 867           271         90 through 339         90 through 200         201 through 337         384         606 through 614         632 through 614         632 through 614         632 through 614         632 through 613         324 through 376         377 through 541         542         739 through 744         761 through 627         731 through 341         332 through 361         377 through 541         542         739 through 635         555 through 666         666 through 632         63 through 632         43 through 377         178 through 342         428         606 through 635         555 through 656         650 through 652         63 through 632         234 through 344         434 through 344         434 through 344         435 through 645         762 through 645         650 through 645	264	42 through 299	42 through 101	102 through 299	300	· -	762 through 775
267   12 through 644   12 through 92   93 through 644   645   1002 through 1007   1020 through 1031	265	198 through 431	198 through 260	261 through 431	432	·	1064 through 1074
268   91 through 459   91 through 330   331 through 459   460     1271 through 1281	266	279 through 473	279 through 362	363 through 473	474	944 through 949	970 through 981
269         70 through 327         70 through 147         148 through 327         328         1741 through 1746         1763 through 1774           270         12 through 497         12 through 104         105 through 497         498         335 through 840         955 through 867           271         39 through 383         90 through 200         201 through 383         384         600 through 614         632 through 649           272         32 through 541         332 through 376         377 through 541         542         738 through 744         761 through 269           273         43 through 222         43 through 177         178 through 221         230 through 535         555 through 566           274         115 through 221         115 through 180         181 through 221         232 dhrough 535         555 through 566           275         232 through 384         232 through 380         181 through 384         385         650 through 655         662 through 673           276         143 through 467         143 through 286         287 through 467         428         606 through 611         628 through 639           277         284 through 463         294 through 384         398 through 671         672         805 through 810         390 through 624           279         63 through 362<	267	12 through 644	12 through 92	93 through 644	645	1002 through 1007	1020 through 1031
270         12 through 497         12 through 104         105 through 497         498         935 through 940         955 through 614         632 through 643           271         90 through 383         90 through 200         201 through 383         384         609 through 614         632 through 643           272         332 through 541         332 through 376         377 through 541         542         739 through 744         761 through 750           273         43 through 222         43 through 222         23         530 through 555         555 through 566           274         115 through 231         115 through 180         181 through 231         232         419 through 424         445 through 455           275         232 through 384         232 through 386         232 through 386         287 through 485         660 through 611         628 through 639           276         143 through 463         294 through 388         398 through 671         672         805 through 611         830 through 640           279         63 through 632         63 through 380         308 through 621         63 through 381         398 through 621         630 through 613         829 through 640           280         12 through 632         21 through 389         398 through 632         631 through 381         382 through 381 </td <td>268</td> <td>91 through 459</td> <td>91 through 330</td> <td>331 through 459</td> <td>460</td> <td>·</td> <td>1271 through 1281</td>	268	91 through 459	91 through 330	331 through 459	460	·	1271 through 1281
271         90 through 383         90 through 200         201 through 383         384         609 through 614         632 through 541           272         332 through 541         332 through 541         332 through 541         542         739 through 744         761 through 773           273         43 through 222         43 through 177         178 through 222         223         530 through 535         555 through 566           274         115 through 231         115 through 180         181 through 231         232         419 through 424         445 through 455           275         232 through 384         232 through 384         385         650 through 651         652 through 639           276         143 through 427         143 through 386         287 through 427         428         606 through 611         628 through 639           277         284 through 663         294 through 384         486         -         762 through 611         622 through 639         293 through 611         622 through 639         830 through 631         830 through 632         838 through 840           279         63 through 362         21 through 362         333         802 through 611	269	70 through 327	70 through 147	148 through 327	328	1741 through 1746	1763 through 1774
272         332 through 541         332 through 376         377 through 541         542         739 through 744         761 through 773           273         43 through 222         43 through 177         178 through 222         223         530 through 535         555 through 566           274         115 through 231         115 through 180         181 through 231         232         419 through 424         445 through 455           275         232 through 384         232 through 286         287 through 427         438 through 655         662 through 673           276         143 through 427         143 through 286         287 through 463         464         -762 through 511         628 through 572           278         182 through 463         294 through 463         398 through 673         660 through 671         182 through 398         399 through 673         693         808 through 813         828 through 840           279         63 through 632         63 through 398         399 through 671         672         805 through 813         828 through 840           280         21 through 362         21 through 364         345 through 525         633         808 through 813         828 through 849           281         21 through 263         21 through 344         345 through 264         365 through 364	270	12 through 497	12 through 104	105 through 497	498	935 through 940	955 through 967
273         43 through 222         43 through 177         178 through 222         223         530 through 535         555 through 566           274         115 through 231         115 through 180         181 through 231         232         419 through 424         445 through 455           275         232 through 384         232 through 300         301 through 384         385         650 through 655         662 through 673           276         143 through 427         143 through 378         380 through 427         428         606 through 611         628 through 639           277         284 through 632         63 through 386         399 through 630         63 through 632         63 through 632         63 through 632         63 through 386         399 through 632         633         808 through 810         830 through 840           280         21 through 362         21 through 362         21 through 362         21 through 362         21 through 363         32 through 362         31 through 364         345 through 503         31 through 364         345 through 503         21 through 364         365 through 503         11 through 344         345 through 503         1504 through 365         16 through 134         135 through 302         63 through 637         1305 through 361         1567 through 367         1587 through 642         660 through 671	271	90 through 383	90 through 200	201 through 383	384	609 through 614	632 through 643
274         115 through 231         115 through 180         181 through 231         292         419 through 424         445 through 455           275         232 through 384         232 through 300         301 through 384         385         650 through 655         662 through 673           276         143 through 427         143 through 427         428         606 through 611         628 through 639           277         284 through 631         284 through 378         380 through 633         464	272	332 through 541	332 through 376	377 through 541	542	739 through 744	761 through 773
275         232 through 384         232 through 300         301 through 884         385         650 through 655         662 through 673           276         143 through 427         143 through 286         287 through 427         428         606 through 611         628 through 639           277         284 through 630         294 through 379         380 through 631         464         -         762 through 772           278         162 through 671         162 through 388         399 through 671         672         805 through 810         830 through 840           279         63 through 632         63 through 308         309 through 632         633         808 through 813         829 through 840           280         21 through 502         21 through 200         201 through 362         363         821 through 826         838 through 849           281         21 through 503         21 through 444         345 through 503         504         1305 through 1310         1330 through 1341           282         3 through 201         1 through 63         64 through 503         105 through 1571         1587 through 671           283         39 through 1034         39 through 134         135 through 204         1035 through 204         660 through 671           284         61 through 285 <t< td=""><td>273</td><td>43 through 222</td><td>43 through 177</td><td>178 through 222</td><td>223</td><td>530 through 535</td><td>555 through 566</td></t<>	273	43 through 222	43 through 177	178 through 222	223	530 through 535	555 through 566
276         143 through 427         143 through 286         287 through 427         428         606 through 611         628 through 639           277         284 through 463         294 through 379         380 through 463         464         -         762 through 772           278         162 through 671         162 through 398         399 through 671         672         805 through 810         830 through 840           279         63 through 632         63 through 308         309 through 632         633         808 through 813         829 through 840           280         21 through 502         21 through 500         201 through 382         363         821 through 826         838 through 849           281         21 through 503         21 through 503         21 through 503         21 through 1310         1330 through 1341           282         1 through 201         1 through 63         64 through 201         202         637 through 642         660 through 671           283         39 through 1034         39 through 134         135 through 201         1035         1566 through 517         1567 through 175         157 th	274	115 through 231	115 through 180	181 through 231	232	419 through 424	445 through 455
277         284 through 463         294 through 379         380 through 631         464         762 through 772           278         162 through 671         162 through 398         399 through 671         672         805 through 810         830 through 840           279         63 through 632         63 through 308         309 through 632         633         808 through 813         829 through 840           280         21 through 362         21 through 200         201 through 362         363         821 through 826         838 through 849           281         21 through 503         21 through 344         345 through 201         202         637 through 642         660 through 671           283         39 through 1034         38 through 134         135 through 1034         1035         1566 through 1571         1587 through 1597           284         69 through 263         69 through 263         69 through 263         264         1173 through 1178         1186 through 1265           285         115 through 265         115 through 204         205 through 382         266         505 through 510         525 through 536           286         90 through 344         90 through 344         345 through 344         345 through 526         505 through 510         551 through 526           287	275	232 through 384	232 through 300	301 through 384	385	650 through 655	662 through 673
278       162 through 671       162 through 398       399 through 671       672       805 through 810       830 through 840         279       63 through 632       63 through 308       309 through 632       633       808 through 613       829 through 840         280       21 through 362       21 through 200       201 through 362       363       821 through 826       838 through 849         281       21 through 503       21 through 344       345 through 503       504       1305 through 642       660 through 671         282       1 through 201       1 through 63       64 through 201       202       637 through 642       660 through 671         283       39 through 1034       39 through 134       135 through 263       264       1173 through 1178       1186 through 1597         284       69 through 263       69 through 125       126 through 263       264       1173 through 1178       1186 through 1205         285       115 through 285       115 through 244       205 through 344       345       500 through 505       515 through 556         286       50 through 344       90 through 140       141 through 344       345       500 through 472       482 through 483         288       96 through 302       96 through 182       183 through 311       312 </td <td>276</td> <td>143 through 427</td> <td>143 through 286</td> <td>287 through 427</td> <td>428</td> <td>606 through 611</td> <td>628 through 639</td>	276	143 through 427	143 through 286	287 through 427	428	606 through 611	628 through 639
279         63 through 632         63 through 308         309 through 632         633         808 through 813         829 through 840           280         21 through 362         21 through 200         201 through 362         363         821 through 826         838 through 849           281         21 through 503         21 through 503         504         1305 through 1310         1330 through 1341           282         1 through 201         1 through 63         64 through 201         202         637 through 642         660 through 671           283         39 through 1034         39 through 134         135 through 263         264         1173 through 1178         1196 through 1205           284         69 through 263         69 through 263         264         1173 through 1178         1196 through 1205           285         115 through 285         115 through 204         205 through 285         286         505 through 510         525 through 526           286         80 through 344         90 through 107         108 through 344         345         500 through 505         515 through 526           287         57 through 311         57 through 107         108 through 311         312         467 through 472         482 through 482           289         161 through 322         161 thro	277	284 through 463	294 through 379	380 through 463	464	•	762 through 772
280         21 through 362         21 through 200         201 through 362         363         821 through 826         838 through 849           281         21 through 503         21 through 503         21 through 503         21 through 503         504         1305 through 1310         1330 through 1341           282         1 through 201         1 through 63         64 through 201         202         637 through 642         660 through 671           283         39 through 1034         39 through 134         135 through 1034         1035         1566 through 1571         1587 through 1597           284         69 through 263         69 through 125         126 through 263         264         1173 through 1178         1186 through 1205           285         115 through 285         115 through 204         205 through 285         286         505 through 510         525 through 526           286         90 through 344         90 through 107         108 through 344         345         500 through 472         482 through 482           287         77 through 311         57 through 120         183 through 302         303         467 through 472         482 through 482         799 through 482         289 through 526         527         799 through 481           289         161 through 322         210 through 3	278	162 through 671	162 through 398	399 through 671	672	805 through 810	830 through 840
21 through 503   21 through 344   345 through 503   504   1305 through 1310   1330 through 1341	279	63 through 632	63 through 308	309 through 632	633	808 through 813	829 through 840
282         1 through 201         1 through 63         64 through 201         202         637 through 642         660 through 671           283         39 through 1034         39 through 134         135 through 1034         1035         1566 through 1571         1587 through 1597           284         69 through 263         69 through 125         126 through 263         264         1173 through 1178         1196 through 1205           285         115 through 265         115 through 328         286         505 through 510         525 through 536           286         90 through 344         90 through 140         141 through 344         345         500 through 505         515 through 527           287         57 through 311         57 through 107         108 through 311         312         467 through 472         482 through 493           288         96 through 302         96 through 182         183 through 302         303         501 through 472         482 through 514           289         161 through 526         161 through 328         329 through 526         527         799 through 611           290         210 through 361         212 through 361         212 through 361         362         650 through 655         673 through 684           292         75 through 631         50 thro	280	21 through 362	21 through 200	201 through 362	363	821 through 826	838 through 849
283         39 through 1034         '39 through 134         135 through 1034         1035         1566 through 1571         1587 through 1597           284         69 through 263         69 through 125         126 through 263         264         1173 through 1178         1196 through 1205           285         115 through 285         115 through 204         205 through 285         286         505 through 510         525 through 536           286         90 through 344         90 through 140         141 through 344         345         500 through 505         515 through 527           287         57 through 311         57 through 107         108 through 311         312         467 through 472         482 through 493           288         96 through 302         96 through 182         183 through 302         303         -         501 through 514           289         161 through 526         161 through 328         329 through 526         527         -         799 through 811           290         210 through 332         210 through 399         300 through 332         333         594 through 599         613 through 625           291         212 through 361         212 through 319         320 through 361         362         650 through 655         673 through 684           292	281	21 through 503	21 through 344	345 through 503	504 ·	1305 through 1310	1330 through 1341
284         69 through 263         69 through 125         126 through 263         264         1173 through 1178         1196 through 1205           285         115 through 285         115 through 204         205 through 285         286         505 through 510         525 through 536           286         90 through 344         90 through 140         141 through 344         345         500 through 505         515 through 527           287         57 through 311         57 through 107         108 through 311         312         467 through 472         482 through 493           288         96 through 302         96 through 182         183 through 302         303         .         501 through 514           289         161 through 526         161 through 328         329 through 526         527         .         799 through 811           290         210 through 332         210 through 299         300 through 332         333         594 through 599         613 through 625           291         212 through 361         212 through 319         320 through 361         362         650 through 655         673 through 684           292         75 through 482         75 through 482         75 through 482         75 through 482         75 through 660         618 through 627           293	282	1 through 201	1 through 63	64 through 201	202	637 through 642	660 through 671
285       115 through 285       115 through 204       205 through 285       286       505 through 510       525 through 536         286       90 through 344       90 through 140       141 through 344       345       500 through 505       515 through 527         287       57 through 311       57 through 107       108 through 311       312       467 through 472       482 through 493         288       96 through 302       96 through 182       183 through 302       303       -       501 through 514         289       161 through 526       161 through 328       329 through 526       527       -       799 through 811         290       210 through 332       210 through 299       300 through 332       333       594 through 599       613 through 625         291       212 through 361       212 through 319       320 through 361       362       650 through 655       673 through 684         292       75 through 482       75 through 482       129 through 482       483       595 through 600       618 through 812         294       154 through 576       154 through 576       577       737 through 742       763 through 775         295       154 through 576       154 through 897       898       1017 through 1022       1044 through 764	283	39 through 1034	'39 through 134	135 through 1034	1035	1566 through 1571	1587 through 1597
286         90 through 344         90 through 140         141 through 344         345         500 through 505         515 through 527           287         57 through 311         57 through 107         108 through 311         312         467 through 472         482 through 493           288         96 through 302         96 through 182         183 through 502         303         -         501 through 514           289         161 through 526         161 through 328         329 through 526         527         -         799 through 811           290         210 through 332         210 through 299         300 through 332         333         594 through 599         613 through 625           291         212 through 361         212 through 319         320 through 361         362         650 through 655         673 through 684           292         75 through 482         75 through 128         129 through 482         483         595 through 600         618 through 627           293         50 through 631         50 through 244         245 through 631         632         777 through 782         801 through 812           294         154 through 576         154 through 360         361 through 576         577         737 through 742         763 through 775           295         154 th	284	69 through 263	69 through 125	126 through 263	264	1173 through 1178	1196 through 1205
287       57 through 311       57 through 107       108 through 311       312       467 through 472       482 through 493         288       96 through 302       96 through 182       183 through 302       303       501 through 514         289       161 through 526       161 through 328       329 through 526       527       799 through 811         290       210 through 332       210 through 299       300 through 332       333       594 through 599       613 through 625         291       212 through 361       212 through 319       320 through 361       362       650 through 655       673 through 684         292       75 through 482       75 through 128       129 through 482       483       595 through 600       618 through 627         293       50 through 631       50 through 244       245 through 631       632       777 through 782       801 through 812         294       154 through 576       154 through 576       577       737 through 742       763 through 775         295       154 through 897       154 through 360       361 through 897       898       1017 through 742       763 through 775         296       146 through 383       126 through 253       254 through 897       898       1017 through 400       433 through 754	285	115 through 285	115 through 204	205 through 285	286	505 through 510	525 through 536
288       96 through 302       96 through 182       183 through 302       303       .       501 through 514         289       161 through 526       161 through 328       329 through 526       527       .       799 through 811         290       210 through 332       210 through 299       300 through 332       333       594 through 599       613 through 625         291       212 through 361       212 through 319       320 through 361       362       650 through 655       673 through 684         292       75 through 482       75 through 128       129 through 482       483       595 through 600       618 through 627         293       50 through 631       50 through 244       245 through 631       632       777 through 782       801 through 812         294       154 through 576       154 through 576       577       737 through 742       763 through 775         295       154 through 897       154 through 360       361 through 897       898       1017 through 1022       1044 through 1054         296       146 through 383       126 through 253       254 through 383       384       726 through 731       743 through 743 through 754         298       66 through 497       66 through 497       66 through 497       498       594 through 737       <	286	90 through 344	90 through 140	141 through 344	345	500 through 505	515 through 527
289       161 through 526       161 through 328       329 through 526       527       .       799 through 811         290       210 through 332       210 through 299       300 through 332       333       594 through 599       613 through 625         291       212 through 361       212 through 319       320 through 361       362       650 through 655       673 through 684         292       75 through 482       75 through 482       483       595 through 600       618 through 627         293       50 through 631       50 through 244       245 through 631       632       777 through 782       801 through 812         294       154 through 576       154 through 360       361 through 576       577       737 through 742       763 through 775         295       154 through 387       154 through 360       361 through 897       898       1017 through 1022       1044 through 1054         296       146 through 292       146 through 253       254 through 292       293       395 through 400       433 through 444         297       126 through 383       126 through 167       168 through 383       384       726 through 731       743 through 754         298       66 through 497       66 through 497       498       594 through 599       618 through 629	287	57 through 311	57 through 107	108 through 311	312	467 through 472	482 through 493
290       210 through 332       210 through 299       300 through 332       333       594 through 599       613 through 625         291       212 through 361       212 through 319       320 through 361       362       650 through 655       673 through 684         292       75 through 482       75 through 128       129 through 482       483       595 through 600       618 through 627         293       50 through 631       50 through 244       245 through 631       632       777 through 782       801 through 812         294       154 through 576       154 through 360       361 through 897       577       737 through 742       763 through 775         295       154 through 897       154 through 360       361 through 897       898       1017 through 1022       1044 through 1054         296       146 through 292       146 through 292       293       395 through 400       433 through 444         297       126 through 383       126 through 167       168 through 383       384       726 through 731       743 through 754         298       66 through 497       66 through 239       240 through 497       498       594 through 599       618 through 628         299       49 through 534       49 through 96       97 through 534       535       593 through 5	288	96 through 302	96 through 182	183 through 302	303	•	501 through 514
291       212 through 361       212 through 319       320 through 361       362       650 through 655       673 through 684         292       75 through 482       75 through 128       129 through 482       483       595 through 600       618 through 627         293       50 through 631       50 through 244       245 through 631       632       777 through 782       801 through 812         294       154 through 576       154 through 360       361 through 897       898       1017 through 1022       1044 through 1054         295       154 through 897       154 through 360       361 through 897       898       1017 through 1022       1044 through 1054         296       146 through 292       146 through 293       254 through 292       293       395 through 400       433 through 444         297       126 through 383       126 through 167       168 through 383       384       726 through 731       743 through 754         298       66 through 497       66 through 239       240 through 497       498       594 through 599       618 through 629         299       49 through 534       49 through 96       97 through 534       535       593 through 598       612 through 623         300       49 through 534       49 through 415       146 through 415 <td< td=""><td>289</td><td>161 through 526</td><td>161 through 328</td><td>329 through 526</td><td>527</td><td></td><td>799 through 811</td></td<>	289	161 through 526	161 through 328	329 through 526	527		799 through 811
292       75 through 482       75 through 128       129 through 482       483       595 through 600       618 through 627         293       50 through 631       50 through 244       245 through 631       632       777 through 782       801 through 812         294       154 through 576       154 through 360       361 through 897       577       737 through 742       763 through 775         295       154 through 897       154 through 360       361 through 897       898       1017 through 1022       1044 through 1054         296       146 through 292       146 through 292       293       395 through 400       433 through 444         297       126 through 383       126 through 167       168 through 383       384       726 through 731       743 through 754         298       66 through 497       66 through 239       240 through 497       498       594 through 599       618 through 629         299       49 through 411       49 through 96       97 through 534       535       593 through 737       750 through 623         300       49 through 534       49 through 96       97 through 534       535       593 through 598       612 through 623         301       86 through 268       56 through 100       101 through 268       269       584 through 589 <td>290</td> <td>210 through 332</td> <td>210 through 299</td> <td>300 through 332</td> <td>333</td> <td>594 through 599</td> <td>613 through 625</td>	290	210 through 332	210 through 299	300 through 332	333	594 through 599	613 through 625
293       50 through 631       50 through 244       245 through 631       632       777 through 782       801 through 812         294       154 through 576       154 through 360       361 through 576       577       737 through 742       763 through 775         295       154 through 897       154 through 360       361 through 897       898       1017 through 1022       1044 through 1054         296       146 through 292       146 through 253       254 through 292       293       395 through 400       433 through 444         297       126 through 383       126 through 167       168 through 383       384       726 through 731       743 through 754         298       66 through 497       66 through 239       240 through 497       498       594 through 599       618 through 629         299       49 through 411       49 through 96       97 through 411       412       732 through 737       750 through 763         300       49 through 534       49 through 96       97 through 534       535       593 through 598       612 through 623         301       86 through 268       56 through 100       101 through 268       269       584 through 589       601 through 612         303       32 through 328       32 through 95       96 through 527       528	291	212 through 361	212 through 319	320 through 361	362	650 through 655	673 through 684
294       154 through 576       154 through 360       361 through 576       577       737 through 742       763 through 775         295       154 through 897       154 through 360       361 through 897       898       1017 through 1022       1044 through 1054         296       146 through 292       146 through 253       254 through 292       293       395 through 400       433 through 444         297       126 through 383       126 through 167       168 through 383       384       726 through 731       743 through 754         298       66 through 497       66 through 239       240 through 497       498       594 through 599       618 through 629         299       49 through 411       49 through 411       412       732 through 737       750 through 763         300       49 through 534       49 through 96       97 through 534       535       593 through 598       612 through 623         301       86 through 415       86 through 415       146 through 415       416       540 through 545       560 through 571         302       56 through 268       56 through 100       101 through 268       269       584 through 589       601 through 539         303       32 through 328       32 through 95       96 through 527       528       921 through 926 <td>292</td> <td>75 through 482</td> <td>75 through 128</td> <td>129 through 482</td> <td>483</td> <td>595 through 600</td> <td>618 through 627</td>	292	75 through 482	75 through 128	129 through 482	483	595 through 600	618 through 627
295       154 through 897       154 through 360       361 through 897       898       1017 through 1022       1044 through 1054         296       146 through 292       146 through 253       254 through 292       293       395 through 400       433 through 444         297       126 through 383       126 through 167       168 through 383       384       726 through 731       743 through 754         298       66 through 497       66 through 239       240 through 497       498       594 through 599       618 through 629         299       49 through 411       49 through 411       412       732 through 737       750 through 763         300       49 through 534       49 through 96       97 through 534       535       593 through 598       612 through 623         301       86 through 415       86 through 145       146 through 415       416       540 through 545       560 through 571         302       56 through 268       56 through 100       101 through 268       269       584 through 589       601 through 612         303       32 through 328       32 through 103       104 through 328       329       508 through 513       528 through 539         304       21 through 527       21 through 95       96 through 527       528       921 through 926	293	50 through 631	50 through 244	245 through 631	632	777 through 782	801 through 812
296       146 through 292       146 through 253       254 through 292       293       395 through 400       433 through 444         297       126 through 383       126 through 167       168 through 383       384       726 through 731       743 through 754         298       66 through 497       66 through 497       498       594 through 599       618 through 629         299       49 through 411       49 through 411       412       732 through 737       750 through 763         300       49 through 534       49 through 96       97 through 534       535       593 through 598       612 through 623         301       86 through 415       86 through 145       146 through 415       416       540 through 545       560 through 571         302       56 through 268       56 through 100       101 through 268       269       584 through 589       601 through 612         303       32 through 328       32 through 103       104 through 328       329       508 through 513       528 through 539         304       21 through 527       21 through 95       96 through 527       528       921 through 926       953 through 963	294	154 through 576	154 through 360	361 through 576	577	737 through 742	763 through 775
297       126 through 383       126 through 167       168 through 383       384       726 through 731       743 through 754         298       66 through 497       66 through 497       498       594 through 599       618 through 629         299       49 through 411       49 through 96       97 through 411       412       732 through 737       750 through 763         300       49 through 534       49 through 96       97 through 534       535       593 through 598       612 through 623         301       86 through 415       86 through 145       146 through 415       416       540 through 545       560 through 571         302       56 through 268       56 through 100       101 through 268       269       584 through 589       601 through 612         303       32 through 328       32 through 103       104 through 328       329       508 through 513       528 through 539         304       21 through 527       21 through 95       96 through 527       528       921 through 926       953 through 963	295	154 through 897	154 through 360	361 through 897	898	1017 through 1022	1044 through 1054
298       66 through 497       66 through 239       240 through 497       498       594 through 599       618 through 629         299       49 through 411       49 through 411       412       732 through 737       750 through 763         300       49 through 534       49 through 96       97 through 534       535       593 through 598       612 through 623         301       86 through 415       86 through 145       146 through 415       416       540 through 545       560 through 571         302       56 through 268       56 through 100       101 through 268       269       584 through 589       601 through 612         303       32 through 328       32 through 103       104 through 328       329       508 through 513       528 through 539         304       21 through 527       21 through 95       96 through 527       528       921 through 926       953 through 963	296	146 through 292	146 through 253	254 through 292	293	395 through 400	433 through 444
299       49 through 411       49 through 96       97 through 411       412       732 through 737       750 through 763         300       49 through 534       49 through 96       97 through 534       535       593 through 598       612 through 623         301       86 through 415       86 through 145       146 through 415       416       540 through 545       560 through 571         302       56 through 268       56 through 100       101 through 268       269       584 through 589       601 through 612         303       32 through 328       32 through 103       104 through 328       329       508 through 513       528 through 539         304       21 through 527       21 through 95       96 through 527       528       921 through 926       953 through 963	297		126 through 167	168 through 383 .	384	726 through 731	743 through 754
300       49 through 534       49 through 96       97 through 534       535       593 through 598       612 through 623         301       86 through 415       86 through 145       146 through 415       416       540 through 545       560 through 571         302       56 through 268       56 through 100       101 through 268       269       584 through 589       601 through 612         303       32 through 328       32 through 103       104 through 328       329       508 through 513       528 through 539         304       21 through 527       21 through 95       96 through 527       528       921 through 926       953 through 963	298	66 through 497	66 through 239		498	594 through 599	618 through 629
301     86 through 415     86 through 145     146 through 415     416     540 through 545     560 through 571       302     56 through 268     56 through 100     101 through 268     269     584 through 589     601 through 612       303     32 through 328     32 through 103     104 through 328     329     508 through 513     528 through 539       304     21 through 527     21 through 95     96 through 527     528     921 through 926     953 through 963	299	49 through 411	49 through 96	97 through 411	412	732 through 737	750 through 763
302       56 through 268       56 through 100       101 through 268       269       584 through 589       601 through 612         303       32 through 328       32 through 103       104 through 328       329       508 through 513       528 through 539         304       21 through 527       21 through 95       96 through 527       528       921 through 926       953 through 963	300	49 through 534	49 through 96	97 through 534	535	593 through 598	612 through 623
303 32 through 328 32 through 103 104 through 328 329 508 through 513 528 through 539 304 21 through 527 21 through 95 96 through 527 528 921 through 926 953 through 963	301	86 through 415	86 through 145	146 through 415	416	540 through 545	560 through 571
304 21 through 527 21 through 95 96 through 527 528 921 through 926 953 through 963	302	56 through 268	56 through 100	101 through 268	269	584 through 589	601 through 612
ORT AND LOUIS AND	303	32 through 328	32 through 103	104 through 328	329	508 through 513	528 through 539
305   147 through 647   147 through 374   375 through 647   648   -   668 through 681	304	21 through 527	21 through 95	96 through 527	528	921 through 926	953 through 963
	305	147 through 647	147 through 374	375 through 647	648	•	668 through 681

CONT. TABLE IV

_	CONT. TABLE IV					•
- [:	306 262 through 471	262 through 306	307 through 471	472	663 through 668	682 through 693
<u> </u>	107 74 through 1216	74 through 172	173 through 1216	1217	1627 through 1632	1640 through 1652
<u> </u>	08 48 through 164	48 through 89	90 through 164	165	482 through 487	505 through 517
<u> </u>	09 185 through 334	185 through 295	296 through 334	335	355 through 360	392 through 405
_	10 195 through 347	195 through 272	273 through 347	348	1037 through 1042	1071 through 1082
<u> </u>	11 90 through 815	90 through 179	180 through 815	816	.883 through 888	905 through 916
<b>—</b>	12 52 through 513	52 through 231	232 through 513	514	553 through 558	572 through 583
. 3	13 172 through 438	172 through 354	355 through 438	439	682 through 687	685 through 697
<u> </u>	14 148 through 366	148 through 225	226 through 366	367	770 through 775	792 through 803
3	15   175 through 336	175 through 276	277 through 336	337	· -	812 through 823
<u> </u>	16 191 through 553	191 through 304	305 through 553	554	766 through 771	804 through 817
3	17 106 through 603	106 through 216	217 through 603	604		1102 through 1112
3	18 47 through 586	47 through 124	125 through 586	587	1583 through 1588	1614 through 1623
3	19 99 through 371	99 through 290	291 through 371	372	491 through 496	513 through 524
32	20 44 through 814	44 through 112	113 through 814	815	1.	978 through 989
32	21 3 through 581	3 through 182	183 through 581	582		1006 through 1016
32	2 107 through 427	107 through 190	191 through 427	428	499 through 504	516 through 529
32	3 45 through 407	45 through 83	84 through 407	408	1008 through 1013	1032 through 1042
32		, 201 through 251	252 through 332	333		869 through 880
32	5 217 through 543	217 through 255	256 through 543	544		1206 through 1217
32		18 through 140	141 through 446	447	930 through 935	948 through 959
32	7 29 through 724	29 through 118	119 through 724	725	886 through 891	910 through 920
32	8 404 through 586	404 through 466	467 through 586	587	1304 through 1309	1334 through 1344
32	9 331 through 432	331 through 387	388 through 432	433	548 through 553	573 through 585
33	0 59 through 703	59 through 220	221 through 703	704	886 through 891	903 through 914
33		672 through 722	723 through 752	753	·	1150 through 1161
33		57 through 128	129 through 311	312	332 through 337	351 through 363
33		80 through 127	128 through 232	233	617 through 622	634 through 645
334		91 through 219	220 through 291	292	367 through 372	389 through 400
33!		196 through 240	241 through 384	385	461 through 466	485 through 496
330		54 through 227	228 through 590	591		955 through 965
337		133 through 345	346 through 846	847		890 through 901
338		138 through 248	249 through 671	672	1319 through 1324	1338 through 1347
339		124 through 186	187 through 411	412	948 through 953	971 through 983
340		372 through 443	444 through 494	495	708 through 713	732 through 745
341		112 through 192	193 through 450	451	1053 through 1058	1095 through 1106
342		117 through 170	171 through 866	867	1159 through 1164	1178 through 1190
343		13 through 75	76 through 465	466	1035 through 1040	1060 through 1070
344		2 through 76	77 through 718	719	1170 through 1175	1203 through 1213
345		86 through 361	362 through 709	710	943 through 948	963 through 973
346		63 through 179	180 through 320	321	771 through 776	799 through 810
347	299 through 418	299 through 379	380 through 418	419	739 through 744	762 through 771
					<u> </u>	

CONT. TABLE IV

CUIT	I. IADLE IV				<u> </u>	
348	186 through 380	186 through 233	234 through 380	381	383 through 388	396 through 409
349	69 through 458	69 through 233	234 through 458	459	564 through 569	602 through 613
350	12 through 638	12 through 263	264 through 638	639	951 through 956	975 through 985
351	282 through 389	282 through 332	333 through 389	390	1413 through 1418	1437 through 1447
352	208 through 339	208 through 294	295 through 339	340	•	1631 through 1641
353	69 through 557	69 through 224	225 through 557	558	849 through 854	870 through 883
354	134 through 325 ·	134 through 274	275 through 325	326		718 through 729
355	78 through 731	78 through 227	228 through 731	732	·	1002 through 1013
356	46 through 693	46 through 90	91 through 693	694	937 through 942	962 through 973
357	126 through 527	126 through 182	183 through 527	528	834 through 839	856 through 867
358	66 through 320	66 through 113	114 through 320	321	490 through 495	508 through 519
359	73 through 948	73 through 159	160 through 948	949	•	1016 through 1028
360	69 through 434	69 through 236	237 through 434	435	419 through 424	441 through 452
361	628 through 804	628 through 711	712 through 804	805	•	864 through 875
362	70 through 366	70 through 108	109 through 366	367	496 through 501	521 through 531
363	70 through 366	70 through 108	109 through 366	367	•	1233 through 1244
364	111 through 434	111 through 185	186 through 434	435		618 through 631
365	19 through 567	19 through 63	64 through 567	568	749 through 754	771 through 781
366	19 through 312	19 through 63	64 through 312	313	896 through 901	921 through 931
367	64 through 612	64 through 234	235 through 612	613	•	839 through 849
368	39 through 458	39 through 80	81 through 458	459	613 through 618	633 through 644
369	9 through 185	9 through 50	51 through 185	186	•	906 through 918
370	14 through 316	14 through 121	122 through 316	317	442 through 447	458 through 471
371	70 through 1092	70 through 234	235 through 1092	1093	1475 through 1480	1493 through 1504
372	274 through 597	274 through 399	400 through 597	598	731 through 736	754 through 765
373	230 through 469	230 through 307	308 through 469	470	1004 through 1009	1027 through 1040
374	72 through 545	72 through 203	204 through 545	546		1151 through 1162
375	36 through 425	36 through 119	120 through 425	426	1215 through 1220	1240 through 1250
376	155 through 751	155 through 340	341 through 751	752	912 through 917	937 through 947
377	46 through 585	46 through 120	121 through 585	586	584 through 589	606 through 619

TABLE V

TABLE V					
ld	Full Length Polypeptide Location	Signal Peptide Location	Mature Polypeptide Location		
141	-31 through 124	-31 through -1	1 through 124		
142	1 through 55		1 through 124		
143	-20 through 47	-20 through -1	1 through 55		
144	21 through 177	-21 through -1	1 through 47		
145	-25 through 110	-25 through -1	1 through 177		
146	-70 through 185	-70 through -1	1 through 110		
147	-49 through 10	-49 through -1	1 through 185		
148	1 through 180	-45 through -1	1 through 10		
149	-23 through 139		1 through 180		
150	-23 through 97	-23 through -1	1 through 139		
151	1 through 7	-23 through -1	1 through 97		
152	-42 through 157	AD through 1	1 through 7		
153	1 through 43	-42 through -1	1 through 157		
154	-37 through 13		1 through 43		
155		-37 through -1	1 through 13		
156	1 through 153		1 through 153		
157	1 through 67	• •	1 through 67		
158	1 through 87	•	1 through 87		
159	-85 through 165	-85 through -1	1 through 165		
160	1 through 24		1 through 24		
	1 through 228		1 through 228		
161	-20 through 66	-20 through -1	1 through 66		
162	1 through 44	•	1 through 44		
163	-58 through 256	-58 through -1	1 through 256		
164	-80 through 9	-80 through -1	1 through 9		
165	-15 through 83	-15 through -1	1 through 83		
166	-36 through 56	-36 through -1	1 through 56		
167	-16 through 335	-16 through -1	1 through 335		
168	-47 through 91	-47 through -1	1 through 91		
169	-73 through 28	-73 through -1	1 through 28		
170	-68 through 184	-68 through -1	1 through 184		
171	-68 through 282	-68 through -1	1 through 282		
172	-68 through 322	-68 through -1	1 through 322		
173	-82 through 108	-82 through -1	1 through 108		
174	-232 through 53	-232 through -1	1 through 53		
175	1 through 153		1 through 153		
176	1 through 49		1 through 49		
177	-24 through 75	-24 through -1	1 through 75		
178	-37 through 58	-37 through -1	1 through 58		
179	-23 through 98	-23 through -1			
180	1 through 59		1 through 98		
181	-14 through 72	-14 through -1	1 through 59		
182	-58 through 107	-58 through -1	1 through 72		
183	-35 through 45	-35 through -1	1 through 107		
184	-21 through 52	-21 through -1	1 through 45		
185	1 through 98	-21 through -1	1 through 52		
186	-21 through 91	-21 through 1	1 through 98		
187	-44 through 26	-21 through -1	1 through 91		
188	-13 through 79	-44 through -1	1 through 26		
189	-42 through 165	-13 through -1	1 through 79		
190	1 through 201	-42 through -1	1 through 165		
	, through 201	<u> </u>	1 through 201		

CONT. TABLE V

CONT. TABL	ΕV		••
191	-37 through 342	-37 through -1	1 through 342
192	1 through 112		1 through 112
193	1 through 43		1 through 43
194	-16 through 35	-16 through -1	1 through 35
195	-18 through 226	-18 through -1	
196	-34 through 319	-34 through -1	1 through 226
197	1 through 30	O T through 1	1 through 319
198	-48 through 64	-48 through -1	1 through 30
199	1 through 54	- To thi bught 1	1 through 64
200	-21 through 130	-21 through -1	1 through 54
201	-25 through 203	-25 through -1	1 through 130
202	-47 through 17	-47 through -1	1 through 203
203	-31 through 115	-31 through -1	1 through 17
204	1 through 87	or through 1	1 through 115
205	-27 through 13	-27 through -1	1 through 87
206	1 through 154	-27 through -1	1 through 13
207	1 through 101	<u> </u>	1 through 154
208	-22 through 434	-22 through -1	1 through 101
209	-17 through 81		1 through 434
210	-29 through 54	-17 through -1	1 through 81
211	-23 through 206	-29 through -1	1 through 54
212	-21 through 131	-23 through -1 -21 through -1	1 through 206
213	-54 through 125	-54 through -1	1 through 131
214	-92 through 177		1 through 125
215	-22 through 113	-92 through -1	1 through 177
216	-38 through 29	-22 through -1	1 through 113
217	-54 through 71	-38 through -1 -54 through -1	1 through 29
218	-21 through 355		1 through 71
219	-30 through 181	-21 through -1 -30 through -1	1 through 355
220	-60 through 94	-60 through -1	1 through 181
221	-42 through 81	-42 through -1	1 through 94
222	-19 through 327	-19 through -1	1 through 81
223	-20 through 190	-20 through -1	1 through 327
224	-20 through 164	-20 through -1	i tilroogii 190
225	-22 through 205	-22 through -1	1 through 164
226	-41 through 33		1 through 205
227	1 through 73	-41 through -1	1 through 33
228	-16 through 66	-16 through -1	1 through 73
229	-56 through 63	-56 through -1	1 through 66
230	1 through 54	-50 timbagh -1	1 through 63
231	-14 through 196	14 through 1	1 through 54
232	1 through 108	-14 through -1	1 through 196
233	-18 through 25	-18 through -1	1 through 108
234	1 through 36	- 10 through -1	1 through 25
235	-13 through 294	12 the	1 through 36
236	-32 through 74	-13 through -1	1 through 294
237	-19 through 23	-32 through -1	1 through 74
238	-20 through 97	·19 through ·1	1 through 23
239	-37 through 141	-20 through -1	1 through 97
240	-27 through 99	-37 through -1	1 through 141
241	-115 through 59	-27 through -1	1 through 99
378	-20 through 32	-115 through -1	1 through 59
379	-23 through 170	-20 through -1	1 through 32
380	-14 through 68	-23 through -1	1 through 170
	7 anough us	-14 through -1	1 through 68

## CONT. TABLE V

<u>ont. Table v</u>			
381	-21 through 177	-21 through -1	1 through 177
382	-55 through 105	-55 through -1	1 through 105
383	-18 through 90	-18 through -1	1 through 90
384	-22 through 42	-22 through -1	1 through 42
385	-15 through 12	-15 through -1	1 through 12
386	-21 through 165	-21 through -1	1 through 165
387	-26 through 153	-26 through -1	1 through 153
388	-55 through 95	-55 through -1	1 through 95
389	-31 through 205	-31 through -1	1 through 205
390	-100 through 49	-100 through -1	1 through 49
391	-49 through 20	-49 through -1	
392	-30 through 211	-30 through -1	1 through 20
393	-30 through 17	-30 through -1	1 through 211
394	-28 through 37	-28 through -1	1 through 17
395	-24 through 49	-24 through -1	1 through 37
396	18 through 42		1 through 49
397	·93 through 99	18 through -1	1 through 42
398	-72 through 77	-93 through -1	1 through 99
399	-20 through 53	-72 through -1	1 through 77
400	-20 through 66	-20 through -1	1 through 53
401	-21 through 57	-20 through -1	1 through 66
402	-28 through 37	21 through 1	1 through 57
403	-27 through 184	-28 through -1	1 through 37
404		-27 through -1	1 through 184
405		·80 through ·1	1 through 43
406	-26 through 60	-26 through -1	1 through 60
407	31 through 131	-31 through -1	1 through 131
408	-37 through 61	-37 through -1	1 through 61
409	-15 through 55	-15 through -1	1 through 55
410	-45 through 15	-45 through -1	1 through 15
411	-22 through 17	-22 through -1	1 through 17
412	-23 through 28	-23 through -1	1 through 28
413	-48 through 47	-48 through -1	1 through 47
414	-32 through 28	-32 through -1	1 through 28
415	-79 through 91	-79 through -1	1 through 91
	-82 through 108	-82 through -1	1 through 108
416	-60 through 54	-60 through -1	1 through 54
417	-108 through 53	-108 through -1	1 through 53
418	-21 through 46	-21 through -1	1 through 46
419	-32 through 300	-32 through -1	1 through 300
420	-19 through 46	-19 through -1	1 through 46
422	-30 through 27	-30 through -1	1 through 27
423	-17 through 68	-17 through -1	1 through 68
424	-17 through 68	-17 through -1	1 through 68
425	-29 through 40	-29 through -1	1 through 40
426	-56 through 66	-56 through -1	1 through 66
427	-30 through 11	-30 through -1	1 through 11
428	-36 through 14	-36 through -1	1 through 14
429	-18 through 118	-18 through -1	1 through 118
430	-65 through 129	-65 through -1	1 through 129
431	-69 through 72	-69 through -1	1 through 72
432	-69 through 179	-69 through -1	1 through 179
433	-36 through 13	-36 through -1	1 through 13
434	-14 through 72	-14 through -1	1 through 72
435	-58 through 86	-58 through -1	1 through 86
			i minondii 90

CONT. TABLE V	•		
436	-16 through 105	-16 through -1	1 through 105
437	-16 through 146	-16 through -1	1 through 146
438	-20 through 90	-20 through -1	
439	-15 through 56	-15 through -1	1 through 90
440	-24 through 75	-24 through -1	1 through 56
441	-25 through 144	-25 through -1	1 through 75
442	-76 through 91	76 through -1	1 through 144
443	-15 through 55	-15 through -1	1 through 91
444	-33 through 348	-33 through -1	1 through 55
445	-14 through 25	-14 through -1	1 through 348
446	-37 through 13	37 through -1	1 through 25
447	-26 through 25	-26 through -1	1 through 13
448	-30 through 212	-30 through -1	1 through 25
449	-60 through 94		1 through 212
450	-61 through 28	-60 through -1	1 through 94
451	-26 through 47	-61 through -1	1 through 28
452		-26 through -1	1 through 47
453	-34 through 20 -38 through 83	-34 through -1	1 through 20
454	-37 through 129	-38 through -1	1 through 83
455	-37 through 129	-37 through -1	1 through 129
456	-64 through 27	-26 through -1	1 through 154
457		-64 through -1	1 through 27
458	-23 through 234	-23 through -1	1 through 234
459	-60 through 133	-60 through -1	1 through 133
460	28 through 79	-28 through -1	1 through 79
460	-13 through 108	-13 through -1	1 through 108
462	-17 through 27	-17 through -1	1 through 27
463	-13 through 96	-13 through -1	1 through 96
464	-41 through 102	-41 through -1	1 through 102
465	-30 through 202	-30 through -1	1 through 202
466	-21 through 40	-21 through -1	1 through 40
467	-19 through 15	-19 through -1	1 through 15
468	-54 through 161	-54 through -1	1 through 161
469	-17 through 10 -24 through 61	-17 through -1	1 through 10
470	· · · · · · · · · · · · · · · · · · ·	-24 through -1	1 through 61
470	-16 through 35	-16 through -1	1 through 35
471	-43 through 24	-43 through -1	1 through 24
473	-15 through 48	-15 through -1	1 through 48
474	-58 through 121	-58 through -1	1 through 121
475	-71 through 167	-71 through -1	1 through 167
	-37 through 141	-37 through -1	1 through 141
476 477	-21 through 75	-21 through -1	1 through 75
477	-24 through 17	-24 through -1	1 through 17
	-27 through 86	-27 through -1	1 through 86
479	-18 through 232	-18 through -1	1 through 232
480	-21 through 130	-21 through -1	1 through 130
481	-25 through 214	-25 through -1	1 through 214
482	-92 through 116	-92 through -1	1 through 116
483	-39 through 47	-39 through -1	1 through 47
484	-27 through 13	-27 through -1	1 through 13
485	-16 through 49	-16 through -1	1 through 49
486	-55 through 75	-55 through -1	1 through 75
487	-84 through 125	-84 through -1	1 through 125
488	-17 through 19	-17 through -1	1 through 19
489	-29 through 15	-29 through -1	1 through 15

# -119-

490	-52 through 111	-52 through -1	4.1.1.2.2.
491	-47 through 17	-47 through -1	1 through 111
492	-50 through 168	-50 through -1	1 through 17
493	-15 through 201		1 through 168
494	-19 through 115	·15 through ·1	1 through 201
495	-16 through 69	-19 through -1	1 through 115
496	-29 through 263	-16 through -1	1 through 69
497	50.1	-29 through -1	1 through 263
498		-56 through -1	1 through 66
499	-28 through 31	-28 through -1	1 through 31
500	-13 through 86	-13 through -1	1 through 86
501	-13 through 86	-13 through -1	1 through 86
	-25 through 83	-25 through -1	1 through 83
502	-15 through 168	-15 through -1	1 through 168
503	-15 through 83	-15 through -1	1 through 83
504	-57 through 126	-57 through -1	1 through 126
505	-14 through 126	-14 through -1	1 through 126
506	-14 through 45	-14 through -1	1 through 45
507	-36 through 65	-36 through -1	
508	-55 through 286	-55 through -1	1 through 65
509	-42 through 66	-42 through -1	1 through 286
510	-26 through 54	-26 through -1	1 through 66
511	-44 through 114	-44 through -1	1 through 54
512	-28 through 102	-28 through -1	1 through 114
513	-62 through 137	-62 through -1	1 through 102
514	25 through 155		1 through 137
		-25 through -1	1 through 155

-120-

TABLE VI

ld	Collection refs	Deposit Name
40	ATCC # 98921	SignalTag 121-144
41	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
42	ATCC # 98921	SignalTag 121-144
43	ATCC # 98920	SignalTag 67-90
44	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
45	ATCC # 98920	SignalTag 67-90
46	ATCC # 98923	SignalTag 44-66
47 .	ATCC # 98920	SignalTag 67-90
48	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
49	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
50	ATCC # 98921	SignalTag 121-144
51	ATCC # 98921	SignalTag 121-144
52	ATCC # 98920	SignalTag 67-90
53	ATCC # 98923	SignalTag 44-66
54	ATCC # 98920	SignalTag 67-90
55	ATCC # 98920	SignalTag 67-90
56	ATCC # 98920	SignalTag 67-90
57	ATCC # 98921	SignalTag 121-144
58	ATCC # 98920	SignalTag 67-90
59	ATCC # 98920	SignalTag 67-90
60	ATCC # 98920	SignalTag 67-90
61	ATCC # 98923	SignalTag 44-66
62	ATCC # 98923	SignalTag 44-66
63	ATCC # 98923	SignalTag 44-66
64	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
65	ATCC # 98923	SignalTag 44-66
66	ATCC # 98921	SignalTag 121-144
67	ATCC # 98920	SignalTag 67-90
68	ATCC # 98920	SignalTag 67-90
69	ATCC # 98921	SignalTag 121-144
70	ATCC # 98921	SignalTag 121-144
71	ATCC # 98921	SignalTag 121-144
72	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
73	ATCC # 98923	SignalTag 44-66
	<del></del>	<u> </u>

74	ATCC # 98923	SignalTag 44-66
75	ATCC # 98920	1
		SignalTag 67-90
76	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
77	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
78	ATCC # 98921	SignalTag 121-144
79	ATCC # 98923	SignalTag 44-66
80	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
81	ATCC # 98921	SignalTag 121-144
82	ATCC # 98920	SignalTag 67-90
83	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
84	ATCC # 98923	SignalTag 44-66
85	ATCC # 98923	SignalTag 44-66
86	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
87	ATCC # 98923	SignalTag 44-66
88	ATCC # 98923	SignalTag 44-66
89	ATCC # 98923	SignalTag 44-66
90	ATCC # 98923	SignalTag 44-66
91	ATCC # 98923	SignalTag 44-66
92	ATCC # 98920	SignalTag 67-90
93	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
94	ATCC # 98923	SignalTag 44-66
95	ATCC # 98923	SignalTag 44-66 :
96	ATCC # 98920	SignalTag 67-90
97	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
98	ATCC # 98921	SignalTag 121-144
99	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
100	ATCC # 98921	SignalTag 121-144
101	ATCC # 98920	SignalTag 67-90
102	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
103	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
104	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
105	ATCC # 98921	SignalTag 121-144
106	ATCC # 98920	SignalTag 67-90
107	ATCC # 98920	SignalTag 67-90
108	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
109	ATCC # 98923	SignalTag 44-66
110	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120

111	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
112	ATCC # 98920	SignalTag 67-90
113	ATCC # 98920	SignalTag 67-90
114	ATCC # 98923	SignalTag 44-66
115	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
116	ATCC,# 98920	SignalTag 67-90
117	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
118	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
119	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
120	. ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
121	ATCC # 98923	SignalTag 44-66
122	ATCC # 98920	SignalTag 67-90
123	ATCC # 98920	SignalTag 67-90
124	ATCC # 98922	SignalTag 91-94, 96, 97, 99-107, 109-112 et 114-120
125	ECACC # 98121506	SignalTag 11121998
126	ECACC # 98121506	SignalTag 11121998
127	ECACC # 98121506	SignalTag 11121998
128	ECACC # 98121506	SignalTag 11121998
129	ECACC # 98121506	SignalTag 11121998
130	ECACC # 98121506	SignalTag 11121998
131	ECACC # 98121506	SignalTag 11121998
132	ECACC # 98121506	SignalTag 11121998
133	ECACC # 98121506	SignalTag 11121998
134	ECACC # 98121506	SignalTag 11121998
135	ECACC # 98121506	SignalTag 11121998
136	ECACC # 98121506	SignalTag 11121998
137	ECACC # 98121506	SignalTag 11121998
138	ECACC # 98121506	SignalTag 11121998
139	ECACC # 98121506	SignalTag 11121998
140	ECACC # 98121506	SignalTag 11121998

-123-

TABLE VII

		•••
Internal designation number	SEO ID NO	Type of sequence
20-5-2-C3-CL0_4	40	DNA
20-8-4-A11-CL2_6	41	DNA
21-1-4-F2-CL11_1	42	DNA
22-11-2-H9-CL1_1	43	DNA
25-7-3-D4-CLO_2	44	DNA
26-27-3-D7-CLO_1	45	DNA
26-35-4-H9-CL1_1	46	DNA
26-45-2-C4-CL2_6	47	DNA
27-1-2-B3-CL0_1	48	DNA
27-1-2-B3-CLO_2	49	DNA
27-19-3-G7-CL11_2	50	DNA
33-10-4-E2-CL13_4	51	DNA
33-10-4-H2-CL2_2	52	DNA
33-110-4-A5-CL1_1	53	DNA
33-13-1-C1-CL1_1	54	DNA
33-30-2-A6-CLO_1	55	DNA
33-35-4-F4-CL1_2	56	DNA
33-35-4-G1-CL1_2	57	DNA
33-36-3-E2-CL1_1	58	DNA
33-36-3-E2-CL1_2	59	DNA
33-36-3-F2-CL2_2	60	DNA
33-4-2-G5-CL2_1	61	DNA
33-49-1-H4-CL1_1	62	DNA
33-66-2-B10-CL4_1	63	DNA
33-97-4-G8-CL2_2	64	DNA
33-98-4-C1-CL1_3	-65	DNA
47-14-1-C3-CL0_5	66	DNA
47-15-1-E11-CLO_1	67	DNA
47-15-1-H8-CLO_2	68	DNA
48-1-1-H7-CLO_1	69	DNA
48-1-1-H7-CLO_4	70	DNA
48-1-1-H7-CLO_5	71	DNA
48-3-1-H9-CLO_6	72	DNA
48-54-1-G9-CL2_1	73	DNA

٠	•124•		
48-54-1-G9-CL3_1	74	DNA	
48-7-4-H2-CL2_2	75	DNA	
51-11-3-D5-CL1_3	76	DNA	
51-11-3-G9-CLO_1	77	DNA	
51-15-4-A12-CL11_3	78	DNA	
51-17-4-A4-CL3_1	79 .	DNA	
51-2-3-F10-CL1_5	80	DNA	
51-2-4-F5-CL11_2	81	DNA	
51-27-4-F2-CL0_2	82	DNA	
51-34-3-F8-CL0_2	83	DNA	
57-1-4-E2-CL1_2	84	DNA	
57-19-2-G8-CL2_1	85	· DNA	
57-27-3-G10-CL2_2	86	DNA	
58-33-3-B4-CL1_2	87	DNA	
58-34-3-C9-CL1_2	88	DNA	
58-4-4-G2-CL2_1	89	DNA	
58-48-1-G3-CL2_4	90	DNA .	
58-6-1-H4-CL1_1	91	DNA	
60-12-1-E11-CL1_2	92	DNA	
65-4-4-H3-CL1_1	93	DNA	
74-5-1-E4-CL1_2	94	DNA	
76-13-3-A9-CL1_2	95	DNA	
76-16-1-D6-CL1_1	96	DNA	
76-28-3-A12-CL1_5	97	DNA	
76-42-2-F3-CLO_1	98	DNA	
77-16-4-G3-CL1_3	99	DNA	
77-39-4-H4-CL11_4	100	DNA	
78-24-3-H4-CL2_1	101	DNA	
78-27-3-D1-CL1_6	102	DNA	
78-28-3-D2-CLO_2	103	DNA	
78-7-1-G5-CL2_6	104	DNA	
84-3-1-G10-CL11_6	105	DNA	
58-48-4-E2-CLO_1	106	DNA	
23-12-2-G6-CL1_2	107	DNA	
25-8-4-B12-CL0_5	108	DNA	
26-44-3-C5-CL2_1	109	DNA	
27-1-2-B3-CLO_3	110	DNA	
L		L	

Ц.,

	· 120·		
30-12-3-G5-CLO_1	111	DNA	
33-106-2-F10-CL1_3	112	DNA	
33-28-4-D1-CLO_1	113	DNA	
33-31-3-C8-CL2_1	114	DNA	
48-24-1-D2-CL3_2	115	DNA	
48-46-4-A11-CL1_4	116	DNA	
51-1-4-C1-CLO_2	117	DNA	
51-39-3-H2-CL1_2	118	DNA	
51-42-3-F9-CL1_1	119	DNA	
51-5-3-G2-CLO_4	120	DNA	
57-18-4-H5-CL2_1	121	DŃA	
76-23-3-G8-CL1_1	122	DNA	
76-23-3-G8-CL1_3	123	DNA	
78-8-3-E6-CLO_1	124	DNA	
19-10-1-C2-CL1_3	125	DNA	
33-11-1-B11-CL1_2	126	DNA	
33-113-2-B8-CL1_2	127	DNA	
33-19-1-C11-CL1_1	128	DNA	
33-61-2-F6-CLO_2	129	DNA	
47-4-4-C6-CL2_2	130	DNA	
48-54-1-G9-CL1_1	131	DNA	
51-43-3-G3-CL0_1	132	DNA	
55-1-3-D11-CLO_1	133	DNA	
58-14-2-D3-CL1_2	134	DNA	
58-35-2-B6-CL2_3	135	DNA	
76-18-1-F6-CL1_1	136	DNA	
76-23-3-G8-CL2_2	137	DNA	
76-30-3-B7-CL1_1	138	DNA	
78-21-3-G7-CL2_1	139	DNA	
58-45-4-B11-CL13_2	140	DNA	
20-5-2-C3-CL0_4	141	PRT	
20-8-4-A11-CL2_6	142	PRT	
21-1-4-F2-CL11_1	143	PRT	
22-11-2-H9-CL1_1	144	PRT	
25-7-3-D4-CL0_2	145	PRT	
26-27-3-D7-CLO_1	146	PRT	
26-35-4-H9-CL1_1	147	PRT	
<del>-</del>		(111	

26-45-2-C4-CL2_6	148	PRT
27-1-2-B3-CLO_1	149	PRT
27-1-2-B3-CLO_2	150	PRT
27-19-3-G7-CL11_2	151	PRT
33-10-4-E2-CL13_4	152	PRT
33-10-4-H2-CL2_2	153	PRT
33-110-4-A5-CL1_1	154	PRT
33-13-1-C1-CL1_1	155	PRT
33-30-2-A6-CLO_1	156	PRT
33-35-4-F4-CL1_2	157	PRT
33-35-4-G1-CL1_2	158	PRT
33-36-3-E2-CL1_1	159	PRT
33-36-3-E2-CL1_2	160	PRT
33-36-3-F2-CL2_2	161	PRT
33-4-2-G5-CL2_1	162	PRT
33-49-1-H4-CL1_1	163	PRT
33-66-2-B10-CL4_1	164	PRT
33-97-4-G8-CL2_2	165	PRT
33-98-4-C1-CL1_3	166	PRT
47-14-1-C3-CLO_5	167	PRT
47-15-1-E11-CLO_1	168	PRT
47-15-1-H8-CLO_2	169	PRT
48-1-1-H7-CLO_1	170	PRT
48-1-1-H7-CL0_4	171	PRT
48-1-1-H7-CL0_5	172	PRT
48-3-1-H9-CLO_6	173	PRT
48-54-1-G9-CL2_1	174	PRT
48-54-1-G9-CL3_1	175	PRT
48-7-4-H2-CL2_2	176	PRT
51-11-3-D5-CL1_3	177	PRT
51-11-3-G9-CLO_1	178	PRT
51-15-4-A12-CL11_3	179	PRT
51-17-4-A4-CL3_1	180	PRT
51-2-3-F10-CL1_5	181	PRT
51-2-4-F5-CL11_2	182	PRT
51-27-4-F2-CLO_2	183	PRT
51-34-3-F8-CLO_2	184	PRT

ابرا

141	•121•	
57-1-4-E2-CL1_2	185	PRT
57-19-2-G8-CL2_1	186	PRT
57-27-3-G10-CL2_2	187	PRT
58-33-3-B4-CL1_2	188	PRT
58-34-3-C9-CL1_2	189	PRT
58-4-4-G2-CL2_1	190	PRT
58-48-1-G3-CL2_4	191	PRT
58-6-1-H4-CL1_1	192	PRT
60-12-1-E11-CL1_2	193	PRT
· 65-4-4-H3-CL1_1	194	PRT
74-5-1-E4-CL1_2	195	PRT
76-13-3-A9-CL1_2	196	PRT
76-16-1-D6-CL1_1	197	PRT
76-28-3-A12-CL1_5	198	PRT
76-42-2-F3-CLO_1	199	PRT
77-16-4-G3-CL1_3	200	PRT
77-39-4-H4-CL11_4	201	PRT
78-24-3-H4-CL2_1	202	PRT
78-27-3-D1-CL1_6	203	PRT
78-28-3-D2-CLO_2	204	PRT
78-7-1-G5-CL2_6	205	PRT
84-3-1-G10-CL11_6	206	PRT
58-48-4-E2-CLO_1	207	PRT
23-12-2-G6-CL1_2	208	PRT
25-8-4-B12-CL0_5	209	PRT
26-44-3-C5-CL2_1	210	PRT
27-1-2-B3-CL0_3	211	PRT
30-12-3-G5-CL0_1	212	PRT
33-106-2-F10-CL1_3	213	PRT
33-28-4-D1-CLO_1	214	PRT
33-31-3-C8-CL2_1	215	PRT
48-24-1-D2-CL3_2	216	PRT
48-46-4-A11-CL1_4	217	PRT
51-1-4-C1-CL0_2	218	PRT
51-39-3-H2-CL1_2	219	PRT
51-42-3-F9-CL1_1	220	PRT
51-5-3-G2-CL0_4	221	PRT

	-128-	
57-18-4-H5-CL2_1	222	PRT
76-23-3-G8-CL1_1	223	PRT
76-23-3-G8-CL1_3	224	PRT
78-8-3-E6-CLO_1	225	PRT
19-10-1-C2-CL1_3	226	PRT
33-11-1-B11-CL1_2	227	PRT
33-113-2-B8-CL1_2	228	PRT
33-19-1-C11-CL1_1	229	PRT
33-61-2-F6-CLO_2	230	PRT .
47-4-4-C6-CL2_2	231	PRT
48-54-1-G9-CL1_1	232	PRT
51-43-3-G3-CL0_1	233	· PRT
55-1-3-D11-CLO_1	234	PRT
58-14-2-D3-CL1_2	235	PRT
58-35-2-B6-CL2_3	236	PRT
76-18-1-F6-CL1_1	237	PRT
76-23-3-G8-CL2_2	238	PRT
76-30-3-B7-CL1_1	239	PRT
78-21-3-G7-CL2_1	240	PRT
58-45-4-B11-CL13_2	241	PRT
20-6-1-D11-FL2	242	DNA
20-8-4-A11-FL2	243	DNA
22-6-2-C1-FL2	244	DNA
22-11-2-H9-FL1	245	DNA
23-8-3-B1-FL1	246	DNA
24-3-3-C6-FL1	247	DNA
24-4-1-H3-FL1	248	DNA
26-45-2-C4-FL2	249	DNA
26-48-1-H10-FL1	250	DNA
26-49-1-A5-FL2	251	DNA
30-6-4-E3-FL3	252	DNA
33-6-1-G11-FL1	253	DNA
33-8-1-A3-FL2	254	DNA
33-11-3-C6-FL1	255	DNA
33-14-4-E1-FL1	256	DNA
33-21-2-D5-FL1	257	DNA
33-26-4-E10-FL1	258	DNA
1		L

33-27-1-E11-FL1	259	DNA
33-28-4-D1-FL1	260	DNA
33-28-4-E2-FL2	261	DNA
33-30-4-C4-FL1	262	DNA
33-35-4-F4-FL1	263	DNA
33-36-3-F2-FL2	264	DNA
33-52-4-F9-FL2	265	DNA
33-52-4-H3-FL1	266	DNA
33-59-1-B7-FL1	267	DNA
33-71-1-A8-FL1	268	DNA
33-72-2-B2-FL1	269	DNA
33-105-2-C3-FL1	270	DNA
33-107-4-C3-FL1	271	DNA
33-110-2-64-FL1	272	DNA
47-7-4-D2-FL2	273	DNA
47-10-2-G12-FL1	274	DNA
47-14-3-D8-FL1	275	DNA
47-18-3-C2-FL1	276	DNA
47-18-3-G5-FL2	277	DNA
47-18-4-E3-FL2	278	DNA
48-3-1-H9-FL3	279	DNA
48-4-2-H3-FL1	280	DNA
48-6-1-C9-FL1	281	DNA
48-7-4-H2-FL2	282	DNA
48-8-1-D8-FL3	283	DNA
48-13-3-H8-FL1	284	DNA
48-19-3-A7-FL1	285	DNA
48-19-3-G1-FL1	286	DNA
48-25-4-D8-FL1	287	DNA
48-21-4-H4-FL1	288	DNA
48-26-3-B8-FL2	289	DNA
48-29-1-E2-FL1	290	DNA
48-31-3-F7-FL1	291	DNA
48-47-3-A5-FL1	292	DNA
51-1-1-G12-FL1	293	DNA
51-1-4-E9-FL3	294	DNA
51-1-4-E9-FL2	295	DNA

130		
296	DNA	
297	DNA	
298	DNA	
299	DNA	
300	DNA	
301	DNA	
302	DNA	
303	DNA	
304	DNA .	
305	DNA	
306	DNA	
307	DNA	
308	DNA	
309	DNA	
310	DNA	
311	DNA	
312	DNA .	
313	DNA	
314	DNA	
315	DNA	
316	DNA	
317	DNA	
318	DNA	
319	DNA	
320	DNA	
321	DNA	
322	DNA	
323	DNA	
324	DNA	
325	DNA	
326	DNA	
327	DNA	
328	DNA	
329	DNA	
330	DNA	
331	DNA	
332	DNA	
	296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 313 314 315 316 317 318 319 320 321 322 323 324 325 326 327 328 329 330 331	

ij,

	•	
65-4-4-H3-FL1	333	DNA
74-3-1-B9-FL1	334	DNA
76-4-1-G5-FL1	335	DNA
76-7-3-A12-FL1	336	DNA
76-16-4-C9-FL3	337	DNA
76-30-3-B7-FL1	338	DNA
77-5-1-C2-FL1	339	DNA
77-5-4-E7-FL1	340	DNA
77-11-1-A3-FL1	341	ONA .
77-16-3-D7-FL1	342	DNA
77-16-4-G3-FL1	343	DNA
77-25-1-A6-FL1	344	DNA
77-26-2-F2-FL3	345	DNA
78-6-2-E3-FL2	346	DNA
78-7-1-G5-FL2	347	DNA
78-16-2-C2-FL1	348	DNA
78-18-3-B4-FL3	349	DNA
78-20-1-G11-FL1	350	DNA
78-22-3-E10-FL1	351	DNA
78-24-2-B8-FL1	352	DNA
78-24-3-A8-FL1	353	DNA
78-24-3-H4-FL2	354	DNA
78-25-1-F11-FL1	355	DNA
78-26-1-B5-FL1	356	DNA
78-27-3-D1-FL1	357	DNA
78-29-1-B2-FL1	358	DNA
78-29-4-B6-FL1	359	DNA
14-1-3-E6-FL1	360	DNA
30-9-1-G8-FL2	361	DNA
33-10-4-H2-FL2	362	DNA
33-10-4-H2-FL1	363	DNA
74-10-3-C9-FL2	364	DNA
33-97-4-G8-FL3	365	DNA
33-97-4-G8-FL2	366	DNA
33-104-4-H4-FL1	367	DNA
47-2-3-B3-FL1	368	DNA
47-37-4-G11-FL1	369	DNA

	•132	<u>/</u> .
57-25-1-F10-FL2	370	DNA
58-19-3-D3-FL1	371	DNA
58-34-3-C9-FL2	372	DNA
58-48-4-E2-FL2	373	DNA
76-21-1-C4-FL1	374	DNA
78-26-2-H7-FL1	375	DNA
77-20-2-E11-FL1	376	DNA
47-1-3-F7-FL2	377	DNA
20-6-1-D11-FL2	378	PRT
20-8-4-A11-FL2	379	PRT
22-6-2-C1-FL2	380	PRT
22-11-2-H9-FL1	381	PRT
23-8-3-B1-FL1	382	PRT
24-3-3-C6-FL1	383	PRT
24-4-1-H3-FL1	384	PRT
26-45-2-C4-FL2	385	PRT
26-48-1-H10-FL1	386	PRT
26-49-1-A5-FL2	387	PRT
30-6-4-E3-FL3	388	PRT
33-6-1-G11-FL1	389	PRT
33-8-1-A3-FL2	390	PRT
33-11-3-C6-FL1	391	PRT
33-14-4-E1-FL1	392	PRT
33-21-2-D5-FL1	393	PRT
33-26-4-E10-FL1	394	PRT
33-27-1-E11-FL1	395	PRT
33-28-4-D1-FL1	396	PRT
33-28-4-E2-FL2	397	PRT
33-30-4-C4-FL1	398	PRT
33-35-4-F4-FL1	399	PRT
33-36-3-F2-FL2	400	PRT
33-52-4-F9-FL2	401	PRT
33-52-4-H3-FL1	402	PRT
33-59-1-B7-FL1	403	PRT
33-71-1-A8-FL1	404	PRT
33-72-2-B2-FL1	405	PRT
33-105-2-C3-FL1	406	PRT
	j l	

-133-		
33-107-4-C3-FL1	407	PRT
33-110-2-G4-FL1	408	PRT
47-7-4-D2-FL2	409	PRT
47-10-2-G12-FL1	410	PRT
47-14-3-D8-FL1	411	PRT
47-18-3-C2-FL1	412	PRT
47-18-3-G5-FL2	413	PRT
47-18-4-E3-FL2	414	PRT
48-3-1-H9-FL3	415	PRT
48-4-2-H3-FL1	416	PRT
48-6-1-C9-FL1	417	PRT
48-7-4-H2-FL2	418	PRT
48-8-1-D8-FL3	419	PRT
48-13-3-H8-FL1	420	PRT
48-19-3-A7-FL1	421	PRT
48-19-3-G1-FL1	422	PRT
48-25-4-D8-FL'1	423	PRT
48-21-4-H4-FL1	424	PRT
48-26-3-B8-FL2	425	PRT
48-29-1-E2-FL1	426	PRT
48-31-3-F7-FL1	427	PRT
48-47-3-A5-FL1	428	PRT
51-1-1-G12-FL1	429	PRT
51-1-4-E9-FL3	430	PRT
51-1-4-E9-FL2	431	PRT
51-2-1-E10-FL1	432	PRT
51-2-3-F10-FL1	433	PRT
51-2-4-F5-FL1	434	PRT
51-3-3-B10-FL2	435	PRT
51-3-3-B10-FL3	436	PRT
51-7-3-G3-FL1	437	PRT
51-10-3-D11-FL1	438	PRT
51-11-3-D5-FL1	439	PRT
51-13-1-F7-FL3	440	PRT
51-15-4-H10-FL1	441	PRT
51-17-4-A4-FL1	442	PRT
51-18-1-C3-FL1	443	PRT

·		104
51-25-3-F3-FL1	444	PRT
51-27-1-E8-FL1	445	PRT
51-28-2-G1-FL2	446	PRT
51-39-3-H2-FL1	447	PRT
51-42-3-F9-FL1	448	PRT
51-44-4-H4-FL1	449	PRT
55-1-3-H10-FL1	450	PRT
55-5-4-A6-FL1	451	PRT
58-26-3-D1-FL1	452	PRT
57-18-1-D5-FL1	453	PRT
57-27-3-A11-FL1	454	PRT
57-27-3-G10-FL2	455	PRT
58-10-3-D12-FL1	456	PRT
58-11-1-G10-FL1	457	PRT
58-11-2-G8-FL2	458	PRT
58-36-3-A9-FL2	459	PRT
58-38-1-A2-FL2	460	PRT .
58-38-1-E5-FL1	461	PRT
58-44-2-B3-FL3	462	PRT
58-45-3-H11-FL1	463	PRT
58-53-2-B12-FL2	464	PRT
59-9-4-A 10-FL1	465	PRT
60-16-3-A6-FL1	466	PRT
60-17-3-G8-FL2	467	PRT
62-5-4-B10-FL1	468	PRT
65-4-4-H3-FL1	469	PRT
74-3-1-B9-FL1	470	PRT
76-4-1-G5-FL1	471	PRT
76-7-3-A12-FL1	472	PRT
76-16-4-C9-FL3	473	PRT
76-30-3-B7-FL1	474	PRT
77-5-1-C2-FL1	475	PRT
77-5-4-E7-FL1	476	PRT
77-11-1-A3-FL1	477	PRT
77-16-3-D7-FL1	478	PRT
77-16-4-G3-FL1	479	PRT
77-25-1-A6-FL1	480	PRT

, Ly

'vi'		
77-26-2-F2-FL3	481	PRT
78-6-2-E3-FL2	482	PRT
78-7-1-G5-FL2	483	PRT
78-16-2-C2-FL1	484	PRT
78-18-3-B4-FL3	485	PRT
78-20-1-G11-FL1	486	PRT
78-22-3-E10-FL1	487	PRT
78-24-2-B8-FL1	488	PRT
78-24-3-A8-FL1	489	PRT .
78-24-3-H4-FL2	490	PRT
78-25-1-F11-FL1	491	PRT
78-26-1-B5-FL1	492	PRT
78-27-3-D1-FL1	493	PRT
78-29-1-B2-FL1	494	PRT
78-29-4-B6-FL1	495	PRT
14-1-3-E6-FL1	496	PRT
30-9-1-G8-FL2	497	PRT
33-10-4-H2-FL2	498	PRT
33-10-4-H2-FL1	499	PRT
74-10-3-C9-FL2	500	PRT
33-97-4-G8-FL3	501	PRT
33-97-4-G8-FL2	502	PRT
33-104-4-H4-FL1	503	PRT
47-2-3-B3-FL1	504	PRT
47-37-4-G11-FL1	505	PRT
57-25-1-F10-FL2	506	PRT
58-19-3-D3-FL1	507	PRT
58-34-3-C9-FL2	508	PRT
58-48-4-E2-FL2	509	PRT
76-21-1-C4-FL1	510	PRT
78-26-2-H7-FL1	511	PRT
77-20-2-E11-FL1	512	PRT
47-1-3-F7-FL2	513	PRT

-136-

# TABLE VIII

ID	Locations	PROSITE Signature Name			
195	110-121	Aldehyde dehydrogenases csyteine active site			
221	28-37	ATP synthase alpha and beta subunits signature			
223	171-181	Regulator of chromosome condensation (RCC1) signature 2			
225	90-112	Phosphatidylethanolamine-binding protein family signature			
226	10-34	Protein kinases ATP-binding region signature			

.

!!

#### WHAT IS CLAIMED IS:

- A purified or isolated nucleic acid comprising the sequence of one of SEQ ID NOs: 40-140 and 242 377 or a sequence complementary thereto.
- 2. A purified or isolated nucleic acid comprising at least 10 consecutive bases of the sequence of one of SEQ ID NOs: 40-140 and 242-377 or one of the sequences complementary thereto.
  - 3. A purified or isolated nucleic acid comprising the full coding sequences of one of SEO ID NOs: 40, 42-44, 46, 48, 49, 51, 53, 60, 62-72, 76-78, 80-83, 85-88, 90, 93, 94, 97, 99-102, 104, 107-125, 127, 132, 135-138, 140 and 242-377wherein the full coding sequence comprises the sequence encoding signal peptide and the sequence encoding mature protein.
- 4. A purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 40-44, 46, 48, 49, 51-53, 55, 56, 58-72, 75-78, 80-88, 90, 93, 94, 97, 99-125, 127, 132, 133, 135-138, 140, and 242-377 which encode a mature protein.
- 5. A purified or isolated nucleic acid comprising the nucleotides of one of SEQ ID NOs: 40, 42-46, 48, 49, 51, 53, 57, 60, 62-73, 76-78, 80-83, 85-88, 90, 93-95, 97, 99-102, 104, 107-125, 127, 128, 130, 132, 134-140
  15 and 242-377 which encode the signal peptide.
  - 6. A purified or isolated nucleic acid encoding a polypeptide having the sequence of one of the sequences of SEQ ID NOs: 141-241 and 378-513.
- 7. A purified or isolated nucleic acid encoding a polypeptide having the sequence of a mature protein included in one of the sequences of SEO ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-20 189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.
  - 8. A purified or isolated nucleic acid encoding a polypeptide having the sequence of a signal peptide included in one of the sequences of SEO ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.
    - 9. A purified or isolated protein comprising the sequence of one of SEO ID NOs: 141-241 and 378-513.
- 25 10. A purified or isolated polypeptide comprising at least 10 consecutive amino acids of one of the sequences of SEO ID NOs: 141-241 and 378-513.
  - 11. An isolated or purified polypeptide comprising a signal peptide of one of the polypeptides of SEQ ID NOs: 141, 143-147, 149, 150, 152, 154, 158, 161, 163-174, 177-179, 181-184, 186-189, 191, 194-196, 198, 200-203, 205, 208-226, 228, 229, 231, 233, 235-241, and 378-513.
- 30 12. An isolated or purified polypeptide comprising a mature protein of one of the polypeptides of SEQ ID NOs: 141-145, 147, 149, 150, 152-154, 156, 157, 159-172, 176-179, 181-189, 191, 194, 195, 198, 200-226, 228, 233, 234, 236-239, 241 and 378-513.
  - 13. A method of making a protein comprising one of the sequences of SEQ ID NO: 141-241 and 378-513, comprising the steps of:

obtaining a cDNA comprising one of the sequences of sequence of SEQ ID NO: 40-140 and 242-377; inserting said cDNA in an expression vector such that said cDNA is operably linked to a promoter; and introducing said expression vector into a host cell whereby said host cell produces the protein encoded by said cDNA.

- 5 14. The method of Claim 13, further comprising the step of isolating said protein.
  - 15. A protein obtainable by the method of Claim 14.
  - 16. A host cell containing a recombinant nucleic acid of Claim 1.
  - 17. A purified or isolated antibody capable of specifically binding to a protein having the sequence of one of SEQ ID NOs: 141-241 and 378-513.
- 10 18. In an array of polynucleotides of at least 15 nucleotides in length, the improvement comprising inclusion in said array of at least one of the sequences of SEQ ID NOs: 40-140 and 242-377, or one of the sequences complementary to the sequences of SEQ ID NOs: 40-140 and 242-377, or a fragment thereof of at least 15 consecutive nucleotides.
- 19. A purified or isolated nucleic acid of at least 15 bases capable of hybridizing under stringent conditions to the sequence of one of SEO ID NOs: 40-140 and 242-377 or a sequence complementary to one of the sequences of SEO ID NOs: 40-140 and 242-377.
  - 20. A purified or isolated antibody capable of binding to a polypeptide comprising at least 10 consecutive amino acids of the sequence of one of SEQ ID NOs: 141-241 and 378-513.

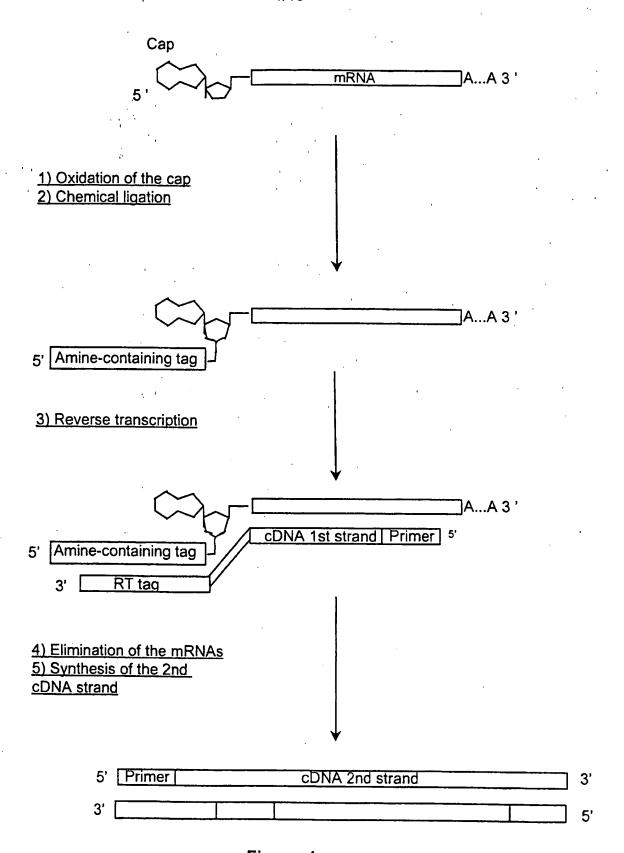
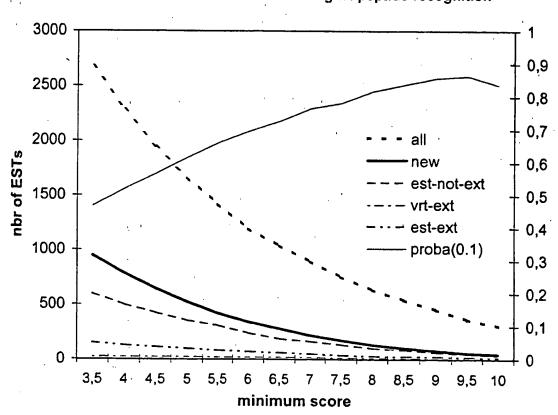


Figure 1

Minimum signal peptide score	false positive rate	false negative rate	proba(0.1)	proba(0.2)
3,5	0,121	0,036	0,467	0,664
4	0,096	0,06	0,519	0,708
4,5	0,078	0,079	0,565	0,745
5	0,062	0,098	0,615	0,782
5,5	0,05	0,127	0,659	0,813
6	0,04	0,163	0,694	0,836
6,5	0,033	0,202	0,725	0,855
7	0,025	0,248	0,763	0,878
7,5	0,021	0,304	0,78	0,889
8	0,015	0,368	0,816	0,909
8,5	0,012	0,418	0,836	0,92
9	0,009	l .	0,856	0,93
9,5	1	1	0,863	0,934
10			0,835	0,919

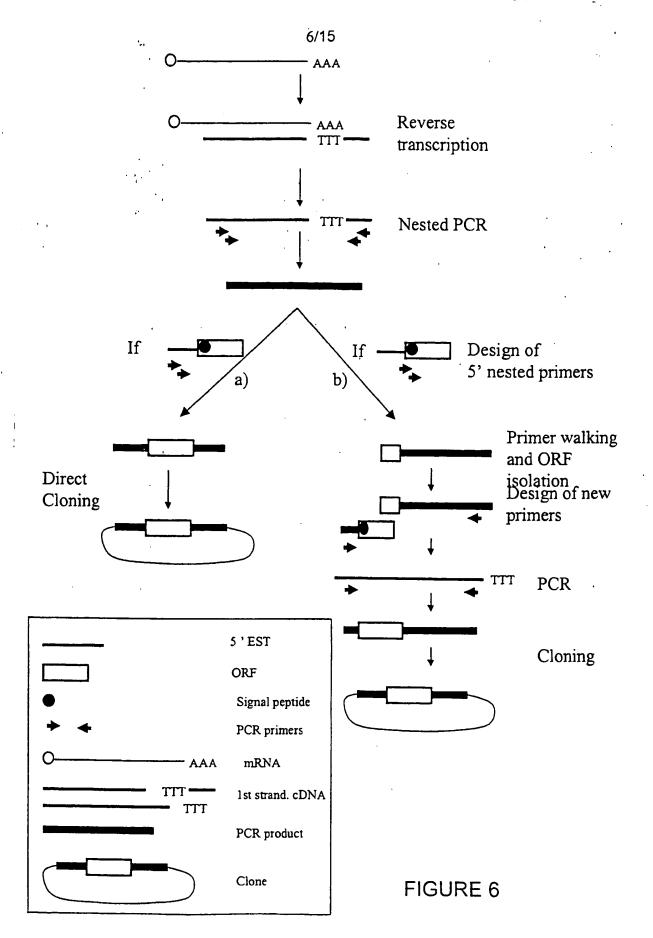
influence of minimum score on signal peptide recognition

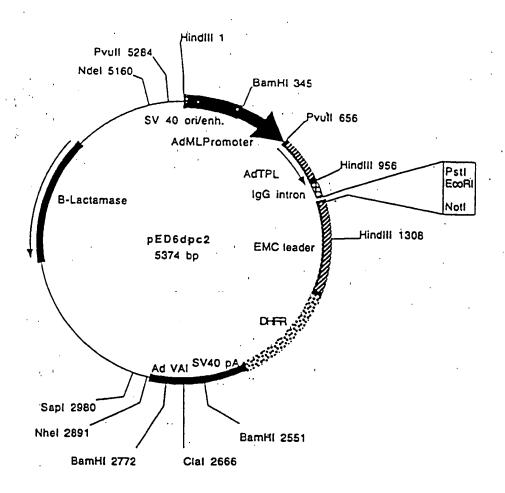


Minimum signal peptide score	All ESTs	New ESTs	ESTs matching public EST closer than 40 bp from	MKNA more	
			beginning	than 40 bp	40 bp
3,5	2674	947	599	. 23	150
4	2278	784	499	23	126
4,5	1943	647	425	22	112
5	1657	523	353	21	96
5,5	1417	419	307	19	80
6	1190	340	238	18	68
6,5	1035	280	186	18	60
7	893	219	161	15	48
7,5	753	173	132	12	36
8	636	133	101	11	29
8,5	543	104	83	8	26
9	456	81	. 63	6	24
9,5	364	57	48	6	18
10	303	47	35	6	·15

	7				
Tissue	All ESTs	New ESTs	ESTs matching public EST closer than	ESTs extending known	ESTs extending public EST
			40 bp from	mRNA more	more than 40
		•	beginning	than 40 bp	bp
Brain	329	131	75	3	24
Cancerous prostate	134	40	37	1	6
Cerebellum	17	9	1	0	. 6
Colon	21	11	4	Ö	ő
Dystrophic muscle	· 41	18	8	0	1
Fetal brain	70	37	16	Ō	1
Fetal kidney	227	116	46	· 1	19
Fetal liver	13	7	2	0	ő
Heart	30	15	7	ō	1
Hypertrophic prostate	86	23	22	2	2
Kidney	10	7	3	0	ō
Large intestine	21	8	4	. 0	1
Liver	23	9	6	0	ó
Lung	24	12	4	Ö	1
Lung (cells)	57	38	6	Ō	4
Lymph ganglia	163	60	23	2	12
Lymphocytes	23	. 6	. 4	ō	2
Muscle	33	16	6	Ö	4
Normal prostate	181	61	45	7	11
Ovary	90	57	12	1	2
Pancreas	48	11	6	0	1
Placenta	24	5	1	0	ó
Prostate	34	16	4	Ö	2
Spleen	56	28	10	Ō	1
Substantia nigra	108	47	27	1	6
Surrenals	15	3	3	1	o
Testis	131	68	25	1	8
Thyroid	17	8	2	o O	2
Umbilical cord	55	17	12	1	3
Uterus	28	15	3	Ö	2
Non tissue-specific	568	48	177	2	28
Total	2677	947	601	23	150

WO 99/31236 PCT/IB98/02122





Plasmid name: pED6dpc2 Plasmid size: 5374 bp



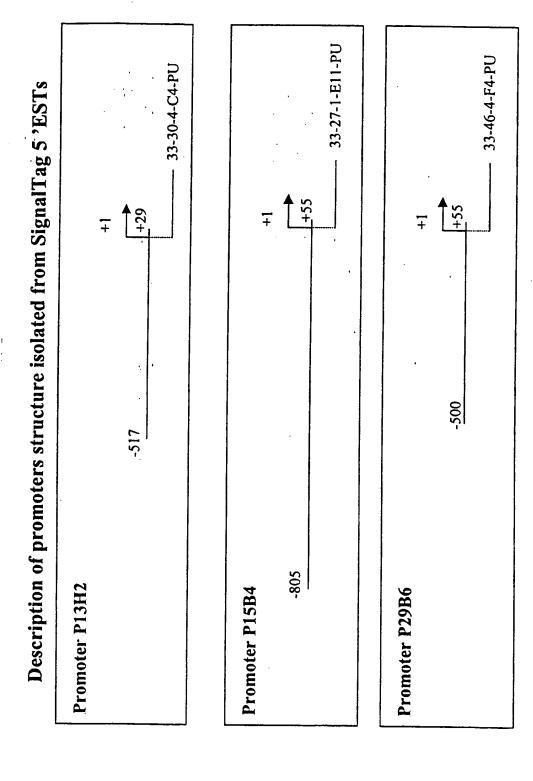


FIGURE 8

9/15

# Description of Transcription Factor Binding Sites present on promoters isolated from SignalTag sequences

#### Promoter sequence P13H2 (546 bp):

Matrix	Position	Orientation	Score	Length	Sequence
CMYB_01	-502	+	0.983	9	TGTCAGTTG
MYOD_Q6	-501	₩.	0.961	10	CCCAACTGAC
S8_01 ·	-444	•	0.960	11	AATAGAATTAG
S8_01	-425	+	0.966	11	AACTAAATTAG
DELTAEF1_01	-390	-	0.960	11	GCACACCTCAG
GATA_C	-364	÷	0.964	11	AGATAAATCCA
CMYB_01	-349	+	0.958	9	CTTCAGTTG
GATA1_02	-343	+'	0.959	14	TTGTAGATAGGAÇA
GATA_C	-339	+'	0.953	11	AGATAGGACAT
TAL1ALPHAE47_01	-235	+	0.973	16	CATAACAGATGGTAAG
TAL1BETAE47_01	-235	+	0.983	16	CATAACAGATGGTAAG
TAL1BETAITF2_01	-235	+	0.978	16	CATAACAGATGGTAAG
MYOD_Q6	-232	•	0.954	• 10	ACCATCTGTT
GATA1_04	-217	•.	0.953	13	TCAAGATAAAGTA
IK1_01	-126	+	0.963	13	AGTTGGGAATTCC
IK2_01	-126	+	0.985	12 🔻	AGTTGGGAATTC
CREL_01	-123	+	0.962	10	TGGGAATTCC
GATA1_02	-96	+	0.950	14	TCAGTGATATGGCA
SRY_02	-41	•	0.951	12	TAAAACAAAACA
E2F_02	-33	+	0.957	8	TTTAGCGC
MZF1_01	-5	•	0.975	, 8	TGAGGGGA

### Promoter sequence P15B4 (861bp):

Matrix	Position	Orientation	Score	Length	Sequence
NFY_Q6	748		0.956	11	GGACCAATCAT
MZF1_01	-738	+	0.962	8	CCTGGGGA
CMYB_01	-684	+	0.994	9	TGACCGTTG
VMYB_02	-682		0.985	. 9	TCCAACGGT
STAT_01	-673	+	0.968	9	TTCCTGGAA
STAT_01	-673	•	0.951	9	TTCCAGGAA
MZF1_01	-556	-	0.956	8	TTGGGGGA
IK2_01	-451	+	0.965	12	GAATGGGATTTC
MZF1_01	-424	+	0.986	8	AGAGGGGA
SRY_02	-398	•	0.955	12	GAAAACAAAACA
MZF1_01	-216	+	0.960	8	GAAGGGGA
MYOD_Q6	-190	+	0.981	10	AGCATCTGCC
DELTAEF1_01	-176	+	0.958	11	TCCCACCTTCC
S8_01	5	-	0.992	11	GAGGCAATTAT
MZF1_01	16	•	0.986	8	AGAGGGGA

## Promoter sequence P29B6 (555 bp):

Matrix	Position	Orientation	Score	Length	Sequence
ARNT_01	-311	+	0.964	16	GGACTCACGTGCTGCT
NMYC_01	-309	+	0.965	12	ACTCACGTGCTG
USF_01	-309	+	0.985	12	ACTCACGTGCTG
USF_01	-309	•	0.985	12	CAGCACGTGAGT
NMYC_01	-309	-	0.956	12	CAGCACGTGAGT
MYCMAX_02	-309	-	0.972	12	CAGCACGTGAGT
USF_C	-307	+	0.997	8	TCACGTGC
USF_C	-307	-	0.991	8	GCACGTGA
MZF1_01	-292	-	0.968	8	CATGGGGA
ELK1_02	-105	+	0.963	14	CTCTCCGGAAGCCT
CETS1P54_01	-102	+	0.974	10	TCCGGAAGCC
AP1_Q4	-42	•	0.963	11	AGTGACTGAAC
AP1FJ_Q2	-42	-	0.961	11	AGTGACTGAAC
PADS_C	45	+	1.000	9	TGTGGTCTC

Figure 9

WO 99/31236 PCT/1B98/02122

10/15

100.0% identity in 125 aa overlap

10 20 30 SEQ ID NO: 217 MADEELEALRRQRLAELQAKHGDPGDAAQQEAKHREAEMRNSILAQVLDQSARARLSNLA SEQ ID NO: 516 MADEELEALRRQRLAELQAKHGDPGDAAQQEAKHREAEMRNSILAQVLDQSARARLSNLA 90 110 120 SEQ ID NO: 217 LVKPEKTKAVENYLIQMARYGQLSEKVSEQGLIEILKKVSQQTEKTTTVKFNRRKVMDSD SEQ ID NO: 516 LVKPEKTKAVENYLIQMARYGQLSEKVSEQGLIEILKKVSQQTEKTTTVKFNRRKVMDSD 70 80 90 100 110 120

SEQ ID NO: 217 EDDDY

::::X

SEQ ID NO: 516 EDDDY

-----

CLUSTAL W(1.5) multiple sequence alignment

SEO ID NO: 517	MFCPLKLILLPVLLDYSLGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLS
SEQ ID NO: 232	MGCVFQSTEDKCIFKIDWTLS
SEQ ID NO: 174	MGCVFQSTEDKRIFKIDWTLS
SEO ID NO: 175	MGCVFQSTVDKCIFKIDWTLS
52Q 1D NO. 175	******* ** *******
	,
SEQ ID NO: 517	DCENTADEAN AAAAN CADICEEONDING NODIN CADCOLL CONODIN
_	PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDNLCNDGSLLLQDVQDVE
SEQ ID NO: 232	PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRL
SEQ ID NO: 174	PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDNLCNDGSLLLQDVQEADQGTYICEIRL
SEQ ID NO: 175	PGEHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRL
	***********
SEQ ID NO: 517	
SEQ ID NO: 232	KGESQVFKKAVVLHVLPEEPKGTQMLT
SEQ ID NO: 174	KGESQVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEE
SEQ ID NO: 175	KGESQVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAK
•	
SEQ ID NO: 517	
SEQ ID NO: 232	
SEQ ID NO: 174	IVFRYYHKLRMSAEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGN
SEQ ID NO: 175	VTRRKHHCVREGSG
SEQ ID NO: 517	
SEQ ID NO: 232	
SEQ ID NO: 174	LVFKKTIVLHVSPEEPRTLVTPAALRPLVLGGNQLVIIVGIVCATILLLPVLILIVKKTC
SEQ ID NO: 174 SEQ ID NO: 175	DVFACTIVEN SPEEKIEVIFAALKPEVEGGNQEVIIVGIVCAIIDELPVLIEIVAKIC
SEQ ID NO: 175	
SEO ID NO: 517	
<del>-</del>	
SEQ ID NO: 232	
SEQ ID NO: 174 SEQ ID NO: 175	GNKSSVNSTVLVKNTKKTNP .

99.6% identity in 225 aa overlap SEQ ID NO: 515 PTAVQKEEARQDVEALLSRTVRTQILTGKELRVATQEKEGSSGRCMLTLLGLSFILAGLI \* SEQ ID NO: 231 LRVATQEKEGSSGRCMLTLLGLSFILAGLI SEQ ID NO: 515 VGGACIYKYFMPKSTIYRGEMCFFDSEDPANSLRGGEPNFLPVTEEADIREDDNIAIIDV SEO ID NO: 231 VGGACIYKYFMPKSTIYRGEMCFFDSEDPANSLRGGEPNFLPVTEEADIREDDNIAIIDV . 60 SEQ ID NO: 515 PVPSFSDSDPAAIIHDFEKGMTAYLDLLLGNCYLMPLNTSIVMPPKNLVELFGKLASGRY SEQ ID NO: 231 PVPSFSDSDPAAIIHDFEKGMTAYLDLLLGICYLMPLNTSIVMPPKNLVELFGKLASGRY SEQ ID NO: 515 LPQTYVVREDLVAVEEIRDVSNLGIFIYQLCNNRKSFRLRRRDLLLGFNKRAIDKCWKIR SEQ ID NO: 231 LPQTYVVREDLVAVEEIRDVSNLGIFIYQLCNNRKSFRLRRRDLLLGFNKRAIDKCWKIR 

250 260

SEQ ID NO: 515 HFPNEFIVETKICQE

SEQ ID NO: 231 HFPNEFIVETKICQE

99.7% identity in 353 aa overlap

070	75	20 306						10	20	30
SEQ	תנ	NO:196		•				SADPRDGTGY		
SEQ	ID	NO:518	LAEGYFDA	AGRLTPEF	SQRLTN	KIRELI		SADPRDGTGY		
			20	30		40	50	60	70	
			и	40	50	ě	60	7.0	0.0	
SEQ	ID	NO:196	•4			LTKRSI	60 TFLCGDAG	70 PLAVAAVLYH	80 KMNNEKOAEI	90 פדדים
			:::::::	:::::::	:::::	::::::	:::::::			::::
SEQ	ID	NO:518				•		PLAVAAVLYH	KMNNEKQA <b>E</b> I	CITR
			80	90	-3	.00	110	120	130'	ı
			1	00	110	1	20	130	140	150
SEQ	ID	NO:196						KTPQSHIQQI	CETILTSGEN	LARK
CEO	TD	NO. E 1 0	:::::::	:::::::	::::::	::::::	::::::::	:.::::::::	:::::::::::::::::::::::::::::::::::::::	::::
SEQ	ידד	NO:316	140	PHAPNEML 150		11ALLF	VNKNFGVE 170	KIPQSHIQQI 180	CETILTSGEN 190	ILARK
		•	,					7		
			_	60	170		80	190 '	200 '	210
SEQ	ID	NO:196						LQVSQGKLHS		
SEQ	ID	NO:518	RNFTAKSP	LMYEWYQE	YYVGAA	HGLAGI	YYYLMOPS	LQVSQGKLHS	LVKPSVDYVO	OLKF
			200	210		20	230	240	250	<b>4</b> - 1 - 1 - 1
				20	230	2	40	252	2.5	
SEQ	ID	NO:196						250 FREEKYLCDA	260 YOCADVIWOY	270 GUUK
			:::::::	::::::	:::::	:::::	:::::::	::::::::::::	::::::::::	::::
SEQ	ID	NO:518						FREEKYLCDA		GLLK
			260	270	2	80	290	300	310	
			_ 2	80	290	3	00	310	320	330
SEQ	ID	NO:196						<b>EWCLEYGEHG</b>		
SEO	TD	NO-518						::::::: EWCLEYGEHG		
			320	330		40	350	360	370	if EGM
SEO	חד	NO-196	3. AGTIYFLA	40 Dilverka	350 DEDNEE	· т.				
224			:::::::							
SEQ	ID	NO:518	AGTIYFLA	DLLVPTKA	RFPAFE	L				
			380	390			•			

PCT/IB98/02122 WO 99/31236

14/15

98.5% identity in 194 aa overlap SEO ID NO:519 ARNLPPLTDAQKNKLRHLSVVTLAAKVKCIPYAVLLEALALRNVRQLEDLVIEAVYADVL SEQ ID NO:158 ARNLPPLTEAQKNKLRHLSVVTLAAKVKCIPYAVLLEALALRNVRQLEDLVIEAVYADVL SEQ ID NO:519 RGSLDQRNQRLEVDYSIGRDIQRQDLSAIAQTLQEWCVGCEVVLSGIEEQVSRANQHKEQ SEQ ID NO:158 RGSLDQRNQRLEVDYSIGRDIQRQDLSAIARTLQEWCVGCEVVLSGIEEQVSRANQHKEQ SEQ ID NO:519 QLGLKQQIESEVANLKKTIKVTTAAAAAATSQDPEQHLTELREPASGTNQRQPSKKASKG SEQ ID NO:158 QLGLKQQIESEVANLKKTIKVTTAAAAAATSQDPEQHLTELREPAPGTNQRQPSKKASKG SEQ ID NO:519 KGLRGSAKIWSKSN SEQ ID NO:158 KGLRGSAKIWSKSN 88.7% identity in 62 aa overlap SEQ ID NO:519 MSAEVKVTGQNQEQFLLLAKSAKGAALATLIHQVLEAPGVYVFGELLDMPNVRELAESDF SEQ ID NO:158 MSAEVKVTGQNQEQFLLLAKSAKGAALATLIHQVLEAPGVYVFGELLDMPNVRELXARNL 

SEQ ID NO:519 AS .x SEQ ID NO:158 PP

68.9% identity in 74 aa overlap 10 20 30 SEQ ID NO:226 MIARRNPVPLRFLPDEARSLPPPKLTDPRLLYIGFLGYCSGLIDNLIRRRPIATAGLHR SEQ ID NO:514 MMTGRQGRATFQFLPDEARSLPPPKLTDPRLAFVGFLGYCSGLIDNAIRRRPVLLAGLHR 10 20 30 40 50 60 70 SEQ ID NO:226 QLLYITAFFLLDIIL SEQ ID NO:514 QLLYITSFVFVGYYLLKRQDYMYAVRDHDMFSYIKSHPEDFPEKDKKTYGEVFEEFHPVR 70 80 90 100 110

. WO 99/31236 PCT/IB98/02122

```
<110> Dumas Milne Edwards, Jean-Baptiste
    Duclert; Aymeric
    Bougueleret, Lydie
```

<120> Extended cDNAS for Secreted Proteins

<130> GENSET.019A

<160> 519

<170> Patent.pm

<210> 1 <211> 47

<212> RNA

<213> Artificial Sequence

<220>

<221> In vitro transcription product

<221> modified\_base

<222> (1)...(1)

<223> m7g

<400> 1

ngcauccuac ucccauccaa uuccacccua acuccuccca ucuccac

47

<210> 2

<211> 46

<212> RNA

<213> Artificial Sequence

<220>

<223> In vitro transcription product

<400> 2

gcauccuacu cccauccaau uccacccuaa cuccucccau cuccac

46

<210> 3

<211> 25

<212> DNA

<213> Artificial Sequence

<220>

<223> In vitro transcription product

<400> 3

atcaagaatt cgcacgagac catta

25

<210> 4

<211> 25

<212> DNA

<213> Artificial Sequence

L <sub>op</sub> ,		
<220> <223> Oligonucleotide		,
<400> 4 taatggtctc gtgcgaattc ttgat		25
taatggtett gtgtgaattt ttgat		
<210> 5	• .	
<211> 25		
<212> DNA	•	
<213> Artificial Sequence		
• •	•	
<220>		1,
<223> Oligonucleotide	•	
<400> 5	•	
ccgacaagac caacgtcaag gccgc		25
p	No. of the second secon	
	W	
<210> 6	n n	
<211> 25		
<212> DNA		
<213> Artificial Sequence		
<220>		
<223> Oligonucleotide		
-	•	
<400> 6		25
tcaccagcag gcagtggctt aggag		25
<210> 7		
<211> 25 <212> DNA		
<213> Artificial Sequence		
value and		
<220>		
<223> Oligonucleotide		
<400> 7		
agtgattcct gctactttgg atggc		25
<210> 8		
<211> 25		
<212> DNA		
<213> Artificial Sequence		
<220>		
<223> Oligonucleotide		
<400> 8		
gcttggtctt gttctggagt ttaga		25

WO 99/31236 -3- PCT/IB98/02122

<211> 25 <212> DNA <213> Artificial Sequence	٠.
<220> <223> Oligonucleotide	
<400> 9 tccagaatgg gagacaagcc aattt	25
<210> 10 <211> 25 <212> DNA	
<213> Artificial Sequence	
<220> <223> Oligonucleotide	. •
<400> 10 agggaggagg aaacagcgtg agtcc	25
<210> 11	
<211> 25	
<212> DNA	
<213> Artificial Sequence	
<220> <223> Oligonucleotide	
(223) Oligonacieotide	
<400> 11	25
atgggaaagg aaaagactca tatca	
<210> 12	. •
<211> 25	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> Oligonucleotide	
<400> 12 agcagcaaca atcaggacag cacag	25
-33	
<210> 13	
<211> 25	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> Oligonucleotide	
<400> 13	25
atcaagaatt cgcacgagac catta	23

<223> blastn

```
<210> 14
<211> 67
<212> DNA
<213> Artificial Sequence
<220>
<223> Oligonucleotide
<400> 14
                                                                         60
atcgttgaga ctcgtaccag cagagtcacg agagagacta cacggtactg gtttttttt
                                                                         67
tttttvn
<210> 15
<211> 29
<212> DNA
<213> Artificial Sequence
<220>
<223> Oligonucleotide
<400> 15
                                                                         29
ccagcagagt cacgagagag actacacgg
<210> 16
<211> 25
<212> DNA
<213> Artificial Sequence
<220>
<223> Oligonucleotide
<400> 16
                                                                         25
cacgagagag actacacggt actgg
<210> 17
<211> 526
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> complement (261..376)
 <223> blastn
 <221> misc_feature
 <222> complement (380..486)
 <223> blastn
 <221> misc_feature
 <222> complement (110..145)
 <223> blastn
 <221> misc_feature
 <222> complement (196..229)
```

-4-

	•
<221> sig_pept'i'de	
<222> 90140	
<223> Von Heijne matrix	
•	
<400> 17	rtcacttoc catttctcat aacagcgtca 60
aatatrarac agctacaata ttccagggcc agagagaaaga actgactgar acgtttgag at	treacting carefully and and a
gagagaaaga actgactgar acgtttgag at	t Lys Lys Val Leu Leu Ile
	-15 -10
aca gcc atc ttg gca gtg gct gtw gg	t ttc cca gtc tct caa gac cag 161
Thr Ala Ile Leu Ala Val Ala Val Gl	y Phe Pro Val Ser Gln Asp Gln
-5	1 5
gaa cga gaa aaa aga agt atc agt ga	ac age gat gaa tta get tea ggr 209
Glu Arg Glu Lys Arg Ser Ile Ser As	sp Ser Asp Glu Leu Ala Ser Gly 20
with the general terms of the contract of the	•
Xaa Phe Val Phe Pro Tyr Pro Tyr Pro	o Phe Arg Pro Leu Pro Pro Ile
25 30	35
cca ttt cca aga ttt cca tgg ttt ag	ga cgt aan ttt cct att cca ata 305
Pro Phe Pro Arg Phe Pro Trp Phe A	rg Arg Xaa Phe Pro Ile Pro Ile
40 45	50 55
cct gaa tot goo cot aca act coo o	tt cct agc gaa aag taaacaaraa 354
Pro Glu Ser Ala Pro Thr Thr Pro L	
60	65 eartgaaart gagccacttc cttgaaraat    414
ggaaaagtca crataaacct ggtcacctga caaaattcct gttaataaaa raaaaacaaa	roraatroaa atagcacaca gcattctcta 474
gtcaatatct ttagtgatct tctttaataa	caccated and and and and and and and and and an
greatatet tragegatet tetteuatuu	
· •	·. '
<210> 18	
<211> 17	
<212> PRT	
<213> Homo sapiens	
<220>	
<221> SIGNAL	
<222> 117	
<223> Von Heijne matrix	
score 8.2	
seq LLLITAILAVAVG/FP	
<400> 18 Met Lys Lys Val Leu Leu Leu Ile T	The Ala Tla Lau Ala Val
_	10 15
1 5 Gly	
017	
<210> 19	
<211> 822	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> misc_feature	
<222> 260464	

<221> misc\_feature <222> 118..184

<223> blastn

<223> blastn 😘 <221> misc\_feature <222> 56..113 <223> blastn <221> misc\_feature <222> 454..485 <223> blastn " <221> misc\_feature <222> 118..545 <223> blastn <221> misc\_feature <222> 65..369 <223> blastn <221> misc\_feature <222> 61..399 <223> blastn <221> misc\_feature <222> 408..458 <223> blastn <221> misc\_feature <222> 60..399 <223> blastn | % " <221> misc\_feature <222> 393..432 <223> blastn <221> sig\_peptide <222> 346..408 <223> Von Heijne matrix <400> 19 actectttta gcataggggc ttcggcgcca gcggccagcg ctagtcggtc tggtaagtgc 60 ctgatgccga gttccgtctc tcgcgtcttt tcctggtccc aggcaaagcg gasgnagatc 120 180 ctcaaacggc ctagtgcttc gcgcttccgg agaaaatcag cggtctaatt aattcctctg gtttgttgaa gcagttacca agaatcttca accctttccc acaaaagcta attgagtaca 240 cgttcctgtt gagtacacgt tcctgttgat ttacaaaagg tgcaggtatg agcaggtctg 300 aagactaaca ttttgtgaag ttgtaaaaca gaaaacctgt tagaa atg tgg tgg ttt 357 Met Trp Trp Phe -20 cag caa ggc ctc agt ttc ctt cct tca gcc ctt gta att tgg aca tct 405 Gln Gln Gly Leu Ser Phe Leu Pro Ser Ala Leu Val Ile Trp Thr Ser -10 gct gct ttc ata ttt tca tac att act gca gta aca ctc cac cat ata 453 Ala Ala Phe Ile Phe Ser Tyr Ile Thr Ala Val Thr Leu His His Ile 10 gac ccg gct tta cct tat atc agt gac act ggt aca gta gct cca raa 501 Asp Pro Ala Leu Pro Tyr Ile Ser Asp Thr Gly Thr Val Ala Pro Xaa 20 25 549 aaa tgc tta ttt ggg gca atg cta aat att gcg gca gtt tta tgt caa Lys Cys Leu Phe Gly Ala Met Leu Asn Ile Ala Ala Val Leu Cys Gln 40 aaa tagaaatcag gaarataatt caacttaaag aakttcattt catgaccaaa 602 ctcttcaraa acatgtcttt acaagcatat ctcttgtatt gctttctaca ctgttgaatt 662

gtctggcaat atttctgcag tggaaaattt gatttarmta gttcttgact gataaatatg gtaaggtggg cttttccccc tgtgtaattg gctactatgt cttactgagc caagttgtaw tttgaaataa aatgatatga gagtgacaca aaaaaaaaaa	722 782 822
<210> 20 <211> 21 <212> PRT	••
<213> Homo sapiens	
<220> <221> SIGNAL	
<222> 121 <223> Von Heijne matrix score 5.5	
seq SFLPSALVIWTSA/AF	
<pre>&lt;400&gt; 20 Met Trp Trp Phe Gln Gln Gly Leu Ser Phe Leu Pro Ser Ala Leu Val 1</pre>	
Ile Trp Thr Ser Ala 20	
<210> 21 <211> 405	
<212> DNA	
<213> Homo sapiens	
<220>	
<pre>&lt;221&gt; misc_feature &lt;222&gt; complement(103398)</pre>	
<223> blastn	
<221> sig_peptide	
<222> 185295 <223> Von Heijne matrix	
<2223> VOII REIJINE MACEIX	
<400> 21 atcaccttct tctccatcct tstctgggcc agtccccarc ccagtccctc tcctgacctg	60
atcagactta agracacat tittatata tagatatta aggatatatt	120
care caretocoma atdatoctco agicocitac aagegoude tygaryayyy	180 229
tggc atg gtg ctg acc acc ctc ccc ttg ccc tct gcc aac age ccc gcg Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val	223
-35 -30 -25	277
aac atg ccc act ggc ccc aac agc ctg agt tat gct agc tct gcc Asn Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala -20 -15 -10	
ctg tcc ccc tgt ctg acc gct cca aak tcc ccc cgg ctt gct atg atg Leu Ser Pro Cys Leu Thr Ala Pro Xaa Ser Pro Arg Leu Ala Met Met	325
-5 1 5 10 cct gac aac taaatatcct tatccaaatc aataaarwra raatcctccc	374
Pro Asp Asn tccaraaggg tttctaaaaa caaaaaaaaa a	40!

<210> 22 <211> 37 <212> PRT

aaacaaaaaa aa

496

```
<213> Homo sapiens
<220>
<221> SIGNAL
<222> 1..37
<223> Von Heijne matrix
      score 5.9
      seq LSYASSALSPCLT/AP
<400> 22
Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val Asn
                5
                                    10
Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala Leu
            20
                                25
                                                     30
Ser Pro Cys Leu Thr
        35
<210> 23
<211> 496
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> 149..331
<223> blastn
<221> misc feature
<222> 328..485
<223> blastn
<221> misc_feature
<222> complement(182..496)
<223> blastn
<221> sig_peptide
<222> 196..240
<223> Von Heijne matrix
<400> 23
                                                                        60
aaaaaattgg tcccagtttt caccetgeeg cagggetgge tggggaggge ageggtttag
                                                                       120
attagccgtg gcctaggccg tttaacgggg tgacacgagc ntgcagggcc gagtccaagg
                                                                       180
cccggagata ggaccaaccg tcaggaatgc gaggaatgtt tttcttcgga ctctatcgag
gcacacagac agacc atg ggg att ctg tct aca gtg aca gcc tta aca ttt
                                                                       231
                 Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe
                                      -10
                  -15
                                                                       279
 gcc ara gcc ctg gac ggc tgc aga aat ggc att gcc cac cct gca agt
 Ala Xaa Ala Leu Asp Gly Cys Arg Asn Gly Ile Ala His Pro Ala Ser
                                                                       327
 gag aag cac aga ctc gag aaa tgt agg gaa ctc gag asc asc cac tcg
 Glu Lys His Arg Leu Glu Lys Cys Arg Glu Leu Glu Xaa Xaa His Ser
                         20
                                              25
     15
 gcc cca gga tca acc cas cac cga aga aaa aca acc aga aga aat tat
                                                                       375
 Ala Pro Gly Ser Thr Xaa His Arg Arg Lys Thr Thr Arg Arg Asn Tyr
                     35
                                                                       424
 tct tca gcc tgaaatgaak ccgggatcaa atggttgctg atcaragccc
 atatttaaat tqqaaaaqtc aaattgasca ttattaaata aagcttgttt aatatgtctc
                                                                       484
```

```
<210> 24
 <211> 15
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> 1..15
 <223> Von Heijne matrix
       score 5.5
       seq ILSTVTALTFAXA/LD
. . . . . .
 <400> 24
 Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe Ala Xaa Ala
                                      10
                  5
 <210> 25
 <211> 623
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> sig_peptide
 <222> 49..96
  <223> Von Heijne matrix
  <400> 25
                                                                         57
  aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg
                                                        Met Glu Arg
                                                            -15
  ctc gtc cta acc ctg tgc acc ctc ccg ctg gct gtg gcg tct gct ggc
                                                                         105
  Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala Ser Ala Gly
              -10
  tgc gcc acg acg cca gct cgc aac ctg agc tgc tac cag tgc ttc aag
                                                                         153
  Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln Cys Phe Lys
                          10
  gtc agc agc tgg acg gag tgc ccg ccc acc tgg tgc agc ccg ctg gac
                                                                         201
  Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser Pro Leu Asp
                                           30
                      25
  caa gtc tgc atc tcc aac gag gtg gtc gtc tct ttt aaa tgg agt gta
                                                                         249
  Gln Val Cys Ile Ser Asn Glu Val Val Val Ser Phe Lys Trp Ser Val
                                       45
                  40
  cgc gtc ctg ctc agc aaa cgc tgt gct ccc aga tgt ccc aac gac aac
                                                                         297
  Arg Val Leu Leu Ser Lys Arg Cys Ala Pro Arg Cys Pro Asn Asp Asn
                                                                         345
  atg aak ttc gaa tgg tcg ccg gcc ccc atg gtg caa ggc gtg atc acc
  Met Xaa Phe Glu Trp Ser Pro Ala Pro Met Val Gln Gly Val Ile Thr
                                                   80
                               75
                                                                         393
  agg cgc tgc tgt tcc tgg gct ctc tgc aac agg gca ctg acc cca cag
  Arg Arg Cys Cys Ser Trp Ala Leu Cys Asn Arg Ala Leu Thr Pro Gln
  gag ggg cgc tgg gcc ctg cra ggg ggg ctc ctg ctc cag gac cct tcg
                                                                         441
  Glu Gly Arg Trp Ala Leu Xaa Gly Gly Leu Leu Gln Asp Pro Ser
                       105
                                           110
  100
  agg ggc ara aaa acc tgg gtg cgg cca cag ctg ggg ctc cca ctc tgc
                                                                         489
  Arg Gly Xaa Lys Thr Trp Val Arg Pro Gln Leu Gly Leu Pro Leu Cys
                                       125
```

ctt ccc awt tcc aac ccc ctc tgc cca rgg gaa acc cag gaa gga

534

WO 99/31236 -10- PCT/IB98/02122 -

Leu Pro Xaa Ser Asn Pro Leu Cys Pro Xaa Glu Thr Gln Glu Gly 135 140 594 taacactgtg ggtgccccca cctgtgcatt gggaccacra cttcaccctc ttggaracaa 623 taaactctca tgcccccaaa aaaaaaaaa <210> 26 <211> 16 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> 1..16 <223> Von Heijne matrix score 10.1 seq LVLTLCTLPLAVA/SA <400> 26 Met Glu Arg Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala 10 <210> 27 <211> 848 <212> DNA <213> Homo sapiens <220> <221> sig\_peptide <222> 32..73 <223> Von Heijne matrix <400> 27 52 aactttgcct tgtgttttcc accctgaaag a atg ttg tgg ctg ctc ttt ttt Met Leu Trp Leu Leu Phe Phe -10 100 ctq qtq act qcc att cat gct gaa ctc tgt caa cca ggt gca gaa aat Leu Val Thr Ala Ile His Ala Glu Leu Cys Gln Pro Gly Ala Glu Asn gct ttt aaa gtg aga ctt agt atc aga aca gct ctg gga gat aaa gca 148 Ala Phe Lys Val Arg Leu Ser Ile Arg Thr Ala Leu Gly Asp Lys Ala 20 196 tat gcc tgg gat acc aat gaa gaa tac ctc ttc aaa gcg atg gta gct Tyr Ala Trp Asp Thr Asn Glu Glu Tyr Leu Phe Lys Ala Met Val Ala 3.0 244 ttc tcc atg aga aaa gtt ccc aac aga gaa gca aca gaa att tcc cat Phe Ser Met Arg Lys Val Pro Asn Arg Glu Ala Thr Glu Ile Ser His 50 292 gtc cta ctt tgc aat gta acc cag agg gta tca ttc tgg ttt gtg gtt Val Leu Leu Cys Asn Val Thr Gln Arg Val Ser Phe Trp Phe Val Val 60 65 340 aca gac cct tca aaa aat cac acc ctt cct gct gtt gag gtg caa tca Thr Asp Pro Ser Lys Asn His Thr Leu Pro Ala Val Glu Val Gln Ser gcc ata aga atg aac aag aac cgg atc aac aat gcc ttc ttt cta aat 388 Ala Ile Arg Met Asn Lys Asn Arg Ile Asn Asn Ala Phe Phe Leu Asn 95 100 gac caa act ctg gaa ttt tta aaa atc cct tcc aca ctt gca cca ccc 436

Asp Gln Thr Leu Glu Phe Leu Lys Ile Pro Ser Thr Leu Ala Pro Pro

	•															
•														120		
				110			<b>.</b>		115	2+2	+++	cat	ata	120 ata	+++	484
atg	gac	cca	tet	gtg Val	CCC	atc	tgg	TIA	Tle	Tle	Dhe	GJV	Val	Tle	Phe	٠.
Met	Asp	Pro	125	vaı	PIO	116	пр	130	116	116	riic	023	135			
+ ~ ~	atc	atc	ata	gtt	gca	att	gca		cta	att	tta	tca		atc	tgg	532
Cvs	Tle	Tle	Ile	Val	Ala	Ile	Ala	Leu	Leu	Ile	Leu	Ser	Gly	Ile	Trp	
cy 5		140					145					150				
caa	cgt	ada	ara	aag	aac	aaa	gaa	cca	tct	gaa	gtg	gat	gac	gct	gaa	580
Gln	Arg	Xaa	Xaa	Lys	Asn	Lys	Glu	Pro	Ser	Glu	Val	Asp	Asp	Ala	Glu	•
	155		•			160					165					<b>620</b>
rat	aak	tgt	gaa	aac	atg	atc	aca	att	gaa	aat	ggc	atc	CCC	TCT	gat	628
Xaa	Xaa	Cys	Glu	Asn		Ile	Thr	He	GIU	Asn	GIY	TTE	Pro	Sei	185	
170			ν.		175					180	~~~	++-	ato	202		676
CCC	ctg	gac	atg	aag Lys	gga	999	Cat	Tla	Acr	yat	Ala	Dhe	Met	Thr	Glu	
Pro	Leu	Asp	met	ьув 190	GIA	GIY	птр	116	195	veb	VIO	- 110	.,	200	,	
			ctc	acc	cct	ctc	taa	aggg		ttati	teta	ct t	cctc		a	727
gat	gag	Arg	Leu	Thr	Pro	Leu	cga.	~955	5			•••				
waħ	GIU	VT. A	205													
att	aaac	att 1	tatt	tctg	tg t	gact	gctg	a gc	atcc	tgaa	ata	ccaa	gag	caga	tcatat	787
wtt	ttgt	ttc	acca	ttct	tc t	tttg	taat	a aa	tttt	gaat	gtg	cttg	aaa	aaaa	aaaaaa	847
С	_															. 848
										•						
		_														
	0 > 2															
	1> 1									•						
	2> P	OMO	cani	270												
<21	3> n	Ollio	2ªbī	CIID							•	•				
<22	0>															
		IGNA	L ·													
		14														
				e ma	trix	:										
		core														
	s	eq L	WLLF	FLVT	AHIA'	/EL										
<40	0> 2	8					_	•	_,		-7.					
	Lev	Trp	Lev	Leu	Phe	Phe	Lev	ı Val		C ATE	1 116	e Hla	s Ale	1		
1				5					10							•
-2.	10> 2	, <b>a</b>														
	11> 2															
	12> I	_														
			icia	al Se	quer	ice										
	-				-											
<2	20>															
<2	23> (	Oligo	onuc!	leoti	ide											
	00> :															25
99	gaag	atgg	agat	tagta	att 9	gcct	3									23

<210> 30 <211> 26 <212> DNA <213> Artificial Sequence <223> Olignucleotide

<400> 30 ctgccatgta catgatagag agattc

26

<210> 31

<211> 546

<212> DNA

<213> Homo sapiens

<220>

<221> promoter

<222> 1..517

<221> transcription start site

<222> 518

<221> protein\_bind

<222> 17..25

<223> matinspector prediction name CMYB\_01 score 0.983 sequence tgtcagttg

<221> protein\_bind

<222> complement (18..27)

<223> matinspector prediction name MYOD\_Q6 score 0.961 sequence cccaactgac

<221> protein\_bind

<222> complement (75..85)

<223> matinspector prediction name S8\_01 score 0.960 sequence aatagaattag

<221> protein\_bind

<222> 94..104

<223> matinspector prediction name S8\_01 score 0.966 sequence aactaaattag

<221> protein\_bind

<222> complement (129..139)

<223> matinspector prediction name DELTAEF1\_01 score 0.960 sequence gcacacctcag

<221> protein\_bind

<222> complement (155..165)

<223> matinspector prediction name GATA\_C score 0.964 sequence agataaatcca

<221> protein\_bind

- <222> 170..178
- <223> matinspector prediction
   name CMYB\_01
   score 0.958
   sequence cttcagttg
- <221> protein\_bind
- <222> 176..189
- <223> matinspector prediction name GATA1\_02 score 0.959 sequence ttgtagataggaca
- <221> protein\_bind
  - <222> 180..190
  - <223> matinspector prediction
     name GATA\_C
     score 0.953
     sequence agataggacat
  - <221> protein\_bind
  - <222> 284..299
  - <223> matinspector prediction
     name TAL1ALPHAE47\_01
     score 0.973
     sequence cataacagatggtaag
  - <221> protein\_bind
  - <222> 284..299
  - <223> matinspector prediction
     name TAL1BETAE47\_01
     score 0.983
     sequence cataacagatggtaag
  - <221> protein\_bind
  - <222> 284..299
  - <223> matinspector prediction
     name TAL1BETAITF2\_01
     score 0.978
     sequence cataacagatggtaag
  - <221> protein\_bind
  - <222> complement (287..296)
  - <223> matinspector prediction name MYOD\_Q6 score 0.954 sequence accatctgtt
  - <221> protein\_bind
  - <222> complement(302..314)
  - <223> matinspector prediction name GATA1\_04 score 0.953 sequence tcaagataaagta
  - <221> protein bind
  - <222> 393..405
  - <223> matinspector prediction name IK1\_01 score 0.963 sequence agttgggaattcc

```
<221> protein_bind
<222> 393..404 +
<223> matinspector prediction
     name IK2 01
      score 0.985
      sequence agttgggaattc
<221> protein bind
<222> 396..405
<223> matinspector prediction
      name CREL 01
      score 0.962
      sequence tgggaattcc
<221> protein_bind
<222> 423..436
<223> matinspector prediction
      name GATA1_02
      score 0.950
      sequence tcagtgatatggca
<221> protein_bind
<222> complement (478..489)
<223> matinspector prediction
      name SRY 02
      score 0.951
      sequence taaaacaaaca
<221> protein_bind
<222> 486..493
<223> matinspector prediction
      name E2F_02
      score 0.957
      sequence tttagcgc
<221> protein bind
<222> complement (514..521)
<223> matinspector prediction
      name MZF1 01
      score 0.975
      sequence tgagggga
<400> 31
                                                                        60
tgagtgcagt gttacatgtc agttgggtta agtttgttaa tgtcattcaa atcttctatg
tettgatttg cetgetaatt etattatte tggaactaaa ttagtttgat ggttetatta
                                                                       120
                                                                       180
gttattgact gaggtgtgct aatctcccat tatgtggatt tatctatttc ttcagttgta
                                                                       240
gataggacat tgatagatac ataagtacca ggacaaaagc agggagatct tttttccaaa
atcaggagaa aaaaatgaca tctggaaaac ctatagggaa aggcataaca gatggtaagg
                                                                       300
atactttatc ttgagtagga gagccttcct gtggcaacgt ggagaaggga agaggtcgta
                                                                       360
gaattgagga gtcagctcag ttagaagcag ggagttggga attccgttca tgtgatttag
                                                                       420
                                                                       480
catcagtgat atggcaaatg tgggactaag ggtagtgatc agagggttaa aattgtgtgt
                                                                       540
tttgttttag cgctgctggg gcatcgcctt gggtcccctc aaacagattc ccatgaatct
cttcat
                                                                       546
```

<210> 32

<211> 23

<212> DNA

<213> Artificial Sequence

23

24

<223> Oligonucleotide <400> 32 gtaccaggga ctgtgaccat tgc <210> 33 <211> 24 <212> DNA <213> Artificial Sequence <220> <223> Oligonucleotide <400> 33 ctgtgaccat tgctcccaag agag <210> 34 <211> 861 <212> DNA <213> Homo sapiens <220> <221> promoter <222> 1..806 <221> transcription start site <222> 807 <221> protein\_bind <222> complement (60..70) <223> matinspector prediction name NFY Q6 score 0.956 sequence ggaccaatcat <221> protein\_bind <222> 70..77 <223> matinspector prediction name MZF1\_01 score 0.962 sequence cctgggga <221> protein\_bind <222> 124..132 <223> matinspector prediction name CMYB 01 score 0.994 sequence tgaccgttg <221> protein bind <222> complement (126..134) <223> matinspector prediction name VMYB\_02 score 0.985 sequence tccaacggt <221> protein\_bind

<222> 135..143

- <223> matinspector prediction name STAT\_01 score 0.968 sequence ttcctggaa
- <221> protein\_bind
- <222> complement (135..143)
- <223> matinspector prediction name STAT\_01 score 0.951 sequence ttccaggaa
- <221> protein\_bind
- <222> complement (252..259)
- <223> matinspector prediction
   name MZF1\_01
   score 0.956
   sequence ttggggga
- <221> protein\_bind
- <222> 357..368
- <223> matinspector prediction ... name IK2\_01 score 0.965 sequence gaatgggatttc
- <221> protein\_bind
- <222> 384..391
- <223> matinspector prediction name MZF1\_01 score 0.986 sequence agaggga
- <221> protein\_bind
- <222> complement (410..421)
- <223> matinspector prediction name SRY\_02 score 0.955 sequence gaaaacaaaaca
- <221> protein\_bind
- <222> 592..599
- <223> matinspector prediction name MZF1\_01 score 0.960 sequence gaaggga
- <221> protein bind
- <222> 618..627
- <223> matinspector prediction name MYOD\_Q6 score 0.981 sequence agcatctgcc
- <221> protein\_bind
- <222> 632..642
- <223> matinspector prediction
   name DELTAEF1\_01
   score 0.958
   seguence tcccaccttcc
- <221> protein\_bind

```
<222> complement(813..823)
<223> matinspector prediction
     name S8 01
     score 0.992
     sequence gaggcaattat
<221> protein_bind
<222> complement(824..831)
<223> matinspector prediction
     name MZF1 01
     score 0.986
     sequence agaggga
<400> 34
tactataggg cacgcgtggt cgacggccgg gctgttctgg agcagagggc atgtcagtaa
                                                                 60
tgattggtcc ctggggaagg tctggctggc tccagcacag tgaggcattt aggtatctct
                                                                120
                                                                180
ctcagagggc taggcacgag ggaaggtcag aggagaaggs aggsarggcc cagtgagarg
                                                                240
ggagcatgcc ttcccccaac cctggcttsc ycttggymam agggcgktty tgggmacttr
                                                                .300
aaytcagggc ccaascagaa scacaggccc aktcntggct smaagcacaa tagcctgaat
                                                                360
420
ccaaatcaag gtaacttgct cccttctgct acgggccttg gtcttggctt gtcctcaccc
                                                                480
agteggaact cectaceact tteaggagag tggttttagg ceegtgggge tgttetgtte
                                                                540
                                                                600
caagcagtgt gagaacatgg ctggtagagg ctctagctgt gtgcggggcc tgaaggggag
                                                                660
tgggttctcg cccaaagagc atctgcccat ttcccacctt cccttctccc accagaagct
                                                                720
tgcctgagct gtttggacaa aaatccaaac cccacttggc tactctggcc tggcttcagc
                                                                780
ttggaaccca atacctaggc ttacaggcca tcctgagcca ggggcctctg gaaattctct
tectgatggt cetttaggtt tgggcacaaa atataattge eteteceete teecatttte
                                                                840
                                                                 861
tctcttggga gcaatggtca c
<210> 35
<211> 20
<212> DNA
<213> Artificial Sequence
<220>
<223> Oligonucleotide
<400> 35
                                                                  20
ctgggatgga aggcacggta
 <210> 36
 <211> 20
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Oligonucleotide
 <400> 36
                                                                  20
 gagaccacac agctagacaa
```

-17-

<210> 37 <211> 555 <212> DNA

<213> Homo sapiens

<220> <221> promoter <222> 1..500 <221> transcription start site <222> 501 <221> protein\_bind <222> 191..206 <223> matinspector prediction name ARNT 01 score 0.964 sequence ggactcacgtgctgct <221> protein\_bind <222> 193..204 <223> matinspector prediction name NMYC 01 score 0.965 sequence actcacgtgctg <221> protein\_bind <222> 193..204 <223> matinspector prediction name USF 01 score 0.985 sequence actcacgtgctg <221> protein\_bind <222> complement (193..204) <223> matinspector prediction name USF 01 score 0.985 sequence cagcacgtgagt <221> protein bind <222> complement (193..204) <223> matinspector prediction name NMYC\_01 score 0.956 sequence cagcacgtgagt <221> protein bind <222> complement (193..204) <223> matinspector prediction name MYCMAX\_02 score 0.972 sequence cagcacgtgagt <221> protein\_bind <222> 195..202 <223> matinspector prediction name USF C score 0.997 sequence tcacgtgc <221> protein\_bind <222> complement (195..202) <223> matinspector prediction

name USF\_C score 0.991

#### sequence gcacgtga

<221> protein\_bind

<222> complement (210..217)

<223> matinspector prediction
 name MZF1\_01
 score 0.968
 sequence catgggga

<221> protein\_bind

<222> 397..410

<223> matinspector prediction
 name ELK1\_02
 score 0.963
 sequence ctctccggaagcct

<221> protein\_bind

<222> 400..409

<223> matinspector prediction name CETS1P54\_01 score 0.974 sequence tccggaagcc

<221> protein\_bind

<222> complement (460..470)

<223> matinspector prediction name AP1\_Q4 score 0.963 sequence agtgactgaac

<221> protein\_bind

<222> complement (460..470)

<223> matinspector prediction
 name AP1FJ\_Q2
 score 0.961
 sequence agtgactgaac

<221> protein\_bind

<222> 547..555

<223> matinspector prediction
 name PADS\_C
 score 1.000
 sequence tgtggtctc

<400> 37 ctatagggca cgcktggtcg acggcccggg ctggtctggt ctgtkgtgga gtcgggttga aggacageat ttgtkacate tggtctactg cacetteeet etgeegtgea ettggeettt 120 kawaagctca gcaccggtgc ccatcacagg gccggcagca cacacatccc attactcaga 180 aggaactgac ggactcacgt gctgctccgt ccccatgagc tcagtggacc tgtctatgta 240 300 gagcagtcag acagtgcctg ggatagagtg agagttcagc cagtaaatcc aagtgattgt 360 catteetgte tgcattagta acteccaace tagatgtgaa aacttagtte ttteteatag gttgctctgc ccatggtccc actgcagacc caggcactct ccggaagcct ggaaatcacc 420 480 cgtgtcttct gcctgctccc gctcacatcc cacacttgtg ttcagtcact gagttacaga ttttgcctcc tcaatttctc ttgtcttagt cccatcctct gttcccctgg ccagtttgtc 540 555 tagctgtgtg gtctc

<210> 38

<211> 19

<212> DNA

<213> Artificial Sequence

-20-

PCT/IB98/02122 WO 99/31236

<220> <223> Oligonucleotide <400> 38 19 ggccatacac ttgagtgac <210> 39 <211> 19 <212> DNA <213> Artificial Sequence <220> <223> Oligonucleotide <400> 39 19 atatagacaa acgcacacc <210> 40 <211> 568 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 7..471 <221> sig\_peptide <222> 7..99 <223> Von Heijne matrix score 6.9 seg LLLVPSALSLLLA/LL <221> polyA\_signal <222> 537..542 <221> polyA\_site <222> 554..568 gggacc atg ttc acc agc acc ggc tcc agt ggg ctc tac aag gcg cct 48 Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro -25 -20 ctg tcg aag agc ctt ctg ctg gtc ccc agt gcc ctc tcc ctc ctg ctc 96 Leu Ser Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu -15 -10 gcc ctc ctc ctg cct cac tgc cag aag ccc ttt gtg tat gac ctt cac 144 Ala Leu Leu Pro His Cys Gln Lys Pro Phe Val Tyr Asp Leu His 192 gca gtc aag aac gac ttc cag att tgg agg ttg ata tgt gga aga ata Ala Val Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile 20 att tgc ctt gat ttg aaa gat act ttc tgc agt agt ctg ctt att tat 240 Ile Cys Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr 35 40 288 aat ttt agg ata ttt gaa aga aga tat gga agc aga aaa ttt gca tcc

Asn Phe Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser

WO 99/31236 -21- PCT/IB98/02122

ttt ttg ctg ggt acc tgg gtt ttg tca gcc tta ttt gac ttt ctc ctc Phe Leu Leu Gly Thr Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu 65 70 75	336
att gaa gct atg cag tat ttc ttt ggc atc act gca gct agt aat ttg Ile Glu Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu 80 85 90 95	384
cct tct gga tta atc ttt tgt tgt gct ttt tgc tct gag act aaa ctc Pro Ser Gly Leu Ile Phe Cys Cys Ala Phe Cys Ser Glu Thr Lys Leu 100 105 110	432
ttc tta tca aga caa gct atg gca gag aac ttt tcc atc taataaattt Phe Leu Ser Arg Gln Ala Met Ala Glu Asn Phe Ser Ile 115. 120	481
aagagtagat tcatctgtat ggttgagagt aggctctgac tatgtatatg tgtataataa acctacatat ccaaaaaaaa aaaaaaa	541 568
<210> 41	
<211> 569	
<212> DNA <213> Homo sapiens	
(213) Nomo Baptens	
<220>	
<221> CDS	
<222> 100332	
<221> polyA_signal <222> 557562	
<400> 41	
agggggcgtg gggccatggt ggtcttgcgg gcggggaaga agacctttct ccccctctc	60
tgccgcgcct tcgcctgccg cggctgtcaa ctcgctccgg agcgcggcgc cgagcgcagg	120
gatacggcgc ccagcggggt cagaaagcaa cattgaatgc agaagaa atg gcg gac Met Ala Asp 1	176
ttc tac aag gaa ttt tta agt aaa aat ttt cag aag cgc atg tat tat Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg Met Tyr Tyr 5 10 15	224
aac aga gat tgg tac aag cgc aat ttt gcc atc acc ttc ttc atg gga Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly 20 25 30 35	272
aaa gtg gcc ctg gaa agg att tgg aac aag ctt aaa cag aaa caa aag	320
Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys 40 45 50	272
aag agg agc aac taggagtcca ctctgaccca gccagagtcc aggtttccac Lys Arg Ser Asn 55	372
aggaagcaga tggagctcct ttcacagggg ctctgagaaa aactggagcc gatctcaaga	432
agccccacat cttcctaagg ggccccatgg cctgtttggg ggcagggtag gtcctggggc	
	492
actgtgggcc gcctgcctgc tgatgtgggc tctaggccag cttgttgtca cgtacgtggt gtgaaataaa gcccaag	492 552 569

<210> 42

<211> 895

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 51..251

<221> sig\_peptide <222> 51..110 <223> Von Heijne matrix score 5.3 seg ALIFGGFISLIGA/AF <221> polyA signal <222> 849..854 <221> polyA\_site. <222> 882..895 <400> 42 ccgagagtgc cgggctggtcg gcgggtcagg gcagcccggg gcctgacgcc atg tcc 56 Met Ser cgg aac ctg cgc acc gcg ctc att ttc ggc ggc ttc atc tcc ctg atc 104 Arg Asn Leu Arg Thr Ala Leu Ile Phe Gly Gly Phe Ile Ser Leu Ile -15 -10 - 5 ggc gcc gcc ttc tat ccc atc tac ttc cgg ccc cta atg aga ttg gag 152 Gly Ala Ala Phe Tyr Pro Ile Tyr Phe Arg Pro Leu Met Arg Leu Glu gag tac aag aag gaa caa gct ata aat cgg gct gga att gtt caa gag 200 Glu Tyr Lys Lys Glu Gln Ala Ile Asn Arg Ala Gly Ile Val Gln Glu 20 25 gat gtg cag cca cca ggg tta aaa gtg tgg tct gat cca ttt ggc agg 248 Asp Val Gln Pro Pro Gly Leu Lys Val Trp Ser Asp Pro Phe Gly Arg 35 40 45 aaa tgagagggct gtcatcagct ctgattaaga aaggagattt cttcatgctt 301 tcgattctgc atggggtaca gccagtcacc tcaccagaga atgacggctg gagaagaaaa 361 ctctgtaata ccataaataa gagtgcttgt aataaaagac tgtgcacaag gattaatatt 421 tecettetta agtateaaaa gaactetgga acaaattata eeattaggaa ggtttteatg 481 attcagttga ttttccaaaa atgaagctat ctcacccagc tgggtttgga ggagcaatct 541 gcttattatt ctgtcgttac cacttactca agcgagctgt gatatgaata caagcaacca 601 gtgggctcgg gaaggtccgg gtctcttctg ccatcttcca gataagagat ttcagtaaaa 661 aactgccatg ctgagctgcc ttatagagct cttcgaaaat gttcgagttg ataaagctct 721 ttgaggacaa ggtacttcgt gcacctcatg ctgaagattg caccatgttg gaagataaat 781 atgaagcaag tcaaactaga tgcatacact tgtgtagaaa tcaataatca attaatagaa 841 895 <210> 43 <211> 691 <212> DNA <213> Homo sapiens

<400> 43

						-20	)			-15						
														ggc		100
	Ala	Met	Val	Thr		Pro	Ala	Ser	Ala	Ala	Pro	Met	Gly	Gly	Pro	
-10					-5		ata	200	cta	1	++0	cat	999	2	cta	148
gaa	CEG	gca	Gln	Tie	Glu	Glu	Leu	Thr	Len	Leu	Phe	His	6] A	acc Thr	Leu	
Giu	Dea	AIU	10	****	014			15					20			
caq	ctg	ggc	cag	gcc	ctc	aac	ggt	gtg	tac	agg	acc	acg	gag	gga	tgg	196
														Gly		
		25					30					35				
														ata		244
Leu		Lys	Ala	Arg	Asn		Leu	GIA	Leu	Tyr	GIY	Arg	Thr	Ile	GIU	
	40	~~~		~~~	a+c	45	caa	aac	caa	gat		acc	cag	gaa	ctt	292
Len	Lev	61v	Gln	Glu	Val	Ser	Ara	Glv	Ara	Asp	Ala	Ala	Gln	Glu	Leu	
55	200				60		5	,	3	65					70	
cgg														cag		340
Arg	Ala	Ser	Leu	Leu	Glu	Thr	Gln	Met	Glu	Glu	Asp	Ile	Leu	Gln	Leu	
				75					80					85		. '
														gca		388
GIn	Ala	GIA	90	Thr	Ala	GIU	val	ьеи 95	GIA	GIU	vaı	Ald	100	Ala	GIII	
220	ata	cta		gac	agc	ata	caq	-	cta	gaa	atc	cad		agg	agc	436
livs	Val	Leu	Ara	Asp	Ser	Val	Gln	Ara	Leu	Glu	Val	Gln	Leu	Arg	Ser	
-2-		105		•			110	_				115		_		
gcc	tgg	ctg	ggc	cct	gcc	tac	cga	gaa	ttt	gag	gtc	tta	aag	gct	cac	484
Ala	_	Leu	Gly	Pro	Ala		Arg	Glu	Phe	Glu		Leu	Lys	Ala	His	
	120					125					130					E22
														gtg		532
135	Asp	гуѕ	GIII	ser	140	116	Deu	тър	MIG	145	1111	Gry	nro	Val	150	
	cag	agg	caa	gag		ata	qca	caq	caq		caa	cta	cqa	cag		580
Arq	Gln	Arq	Arq	Glu	Met	Val	Ala	Gln	Gln	His	Arg	Leu	Arg	Gln	Ile	
5			_	155					160		_			165		
												atct	gcc	tgga	tggaac	633
Gln	Glu	Arg		His	Thr	Ala	Ala		Pro	Ala						
			170					175			<b>.</b>	~~		a+~-	2000	691
tga	ggac	caa	tcat	gctg	ca a	ggaa	cact	t CC	acgc	cccg	tga	ggcc	CCE	gtgc	<u> </u>	031

<210> 44

<211> 458

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 12..416

<221> sig\_peptide

<222> 12..86

<223> Von Heijne matrix score 4

seq LVVMVPLVGLIHL/GW

<221> polyA\_signal

<222> 425..430

<221> polyA\_site

<222> 445..458

-400> 44 W	
<pre>&lt;400&gt; 44</pre>	50
Met Ser Leu Arg Asn Leu Trp Arg Asp Tyr Lys Val Leu -25 -20 -15	٠.
gtt gtt atg gtc cct tta gtt ggg ctc ata cat ttg ggg tgg tac aga	98
Val Val Met Val Pro Leu Val Gly Leu Ile His Leu Gly Trp Tyr Arg -10 -5 1	
atc aaa agc agc cct gtt ttc caa ata cct aaa aac gac gac att cct	146
Ile Lys Ser Ser Pro Val Phe Gln Ile Pro Lys Asn Asp Asp Ile Pro	
5 10 15 20	
gag caa gat agt ctg gga ctt tca aat ctt cag aag agc caa atc cag	194
Glu Gln Asp Ser Leu Gly Leu Ser Asn Leu Gln Lys Ser Gln Ile Gln 25 30 35	
ggg aag nta gca ggc ttg caa tct tca ggt aaa gaa gca gct ttg aat	242
Gly Lys Xaa Ala Gly Leu Gln Ser Ser Gly Lys Glu Ala Ala Leu Asn	
40 45 50	
ctg agc ttc ata tcg aaa gaa gag atg aaa aat acc agt tgg att aga	290
Leu Ser Phe Ile Ser Lys Glu Glu Met Lys Asn Thr Ser Trp Ile Arg	
55 60 65	
aag aac tgg ctt ctt gta gct ggg ata tct ttc ata ggt gac cat ctt	338
Lys Asn Trp Leu Leu Val Ala Gly Ile Ser Phe Ile Gly Asp His Leu	
70 75 80	
gga aca tac ttt ttg cag agg tct gca aag cag tct gta aaa ttt cag	386
Gly Thr Tyr Phe Leu Gln Arg Ser Ala Lys Gln Ser Val Lys Phe Gln	
85 90 95 100	
tct caa agc aaa caa aag agt att gaa gag tgaagtaaaa taaatatttg	436
Ser Gln Ser Lys Gln Lys Ser Ile Glu Glu	
105 110	450
gaattactaa aaaaaaaaaa aa	458
010. 45	
<210> 45 <211> 2036	
<211> 2036 <212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> CDS	
\LLL\(\rightarrow\) \(\rightarrow\) \(\rightar	
<221> sig_peptide	
<222> 276485	
<223> Von Heijne matrix	
score 3.9	
seg SVIGVMLAPFTAG/LS	
<221> polyA site	
<222> 20242036	
<400> 45	
gatectgggt geageteate acaagegteg gggtgeagea aaaceateea ggetggacag	60
tggctggaca gttccaagaa aagaaacgct tcaccgaaga agtcattgaa tacttccaga	120
agaaagttag cccagtgcat ctgaaaatcc tgctgactag cgatgaagcc tggaagagat	180
tcgtgcgtgt ggctggattg cccagggaag aagcagatgc tctctatgaa gctctgaaga	240
atcttacacc atatgtggct attgaggaca aagac atg cag caa aaa gaa cag	293
Met Gln Gln Lys Glu Gln	
-70 -65	
cag ttt agg gag tgg ttt ttg aaa gag ttt cct caa atc aga tgg aag	341
Gln Phe Arg Glu Trp Phe Leu Lys Glu Phe Pro Gln Ile Arg Trp Lys	
-60 -55 -50	
	200

att cag gag too ata gaa agg ott ogt gto att gca aat gag att gaa

389

WO 99/31236 -25- PCT/IB98/02122

			-45					-40					Glu -35			
aaσ	atc	cac	aga	qqc	tgc	gtc	atc	gcc	aat	gtg	gtg	tct	ggc	tcc.	act	437
Ivs	Val	His	Arg	Glv	Cvs	Val	Ile	Ala	Asn	Val	Val	Ser	Gly	Ser	Thr	
<b>_</b>		-30	3	,	4		-25					-20	_			
~~~	atc		tct	atc	att	aac	att	ato	tta	aca	cca	ttt	aca	qca	ggg	485
990	710	Tan	505	77-1	Tle	220	Val	Met	T.em	Δla	Pro	Phe	Thr	Ala	Glv	
GIY		nea	361	vai	116	-10	VAI	Mec	БСи	niu	-5				<b>-</b> -7	. •
	-15							~~~	~+ >	~~~	-	000	2+2	ac=	tet	533
ctg	agc	ctg	agc	att	act	gca	900	999	yıa	999	Tan	994	ata	NIA	Cor	
Leu	Ser	Leu	ser		Thr	Ala	ATS	GIA		GIÀ	Leu	Gry	Ile		261	
1			i t	5					10					15		581
gcc	acg	gct	<b>a</b> aa	atc	gcc	tcc	agc	atc	gtg	gag	aac	aca	tac	aca	agg	201
Ala	Thr	Ala		Ile	Ala	Ser	Ser		Val	GIU	Asn	Thr	Tyr	Thr	Arg	
50			20					25					30			620
tca	gca	gaa	ctc	aca	gcc	agc	agg	ctg	act	gca	acc	agc	act	gac	caa	629
Ser	Ala	Glu	Leu	Thr	Ala	Ser	Arg	Leu	Thr	Ala	Thr		Thr	Asp	GID	• •
		35					40					45				4
ttg	gag	gca	tta	agg	gac	att	ctg	cat	gac	atc	aca	ccc	aat	gtg	ctt	677
Leu	Glu	Ala	Leu	Arg	Asp	Ile	Leu	His	Asp	Ile	Thr	Pro	Asn	Val	Leu	•
	50					55					60					
tcc	ttt	gca	ctt	gat	ttt	gac	gaa	gcc	aca	aaa	atg	att	gcg	aat	gat	725
Ser	Phe	Ala	Leu	Asp	Phe	Asp	Glu	Ala	Thr	Lys	Met	Ile	Ala	Asn	Asp	
65				•	70	•				75					80	
	cat	aca	ctc	agg	aga	tct	aaa	qcc	act	gtt	gga	cgc	cct	ttg	att	773
Val	His	Thr	Leu	Arg	Ara	Ser	Lvs	Ala	Thr	Val	Gly	Arg	Pro	Leu	Ile	
V 4.1				85	5		-2-	,	90		•	_		95		
act	taa	cas	tat		cct	ata	aat	att		gag	aca	cta	aga	aca	cat	821
212	T-5	720	Tur	Val	Dro	Tle	Acn	Val	Val	Glu	Thr	Leu	Arg	Thr	Arg	
Wlq	пр	Arg	100	VAI	FIU	110	71011	105					110		<b>J</b>	
					-+-	a+ a	202			acc	caa	880	ctg		aaq	869
999	gcc	200	acc	299	71-	919	aya Nea	Tur	y.a	שנים	720	) aac	Leu	Glv	Lve	
GIA	Ala		THE	Arg	116	vaı	120		Val	VIO	, AI 9	125		019	2,2	
		115									~+ c			ata	C22	917
gcc	act	tca	ggt	gtc	Ctc	911	919	Tav	yat	yea	17-1	700	TON	77-3	caa Gln	<i>y</i> = <i>i</i>
Ala		Ser	GIY	Val	ren			пеп	Asp	Val			. Deu	Val	Gln	
	130					135					140			<b>~~~</b>	++-	965
gac	tca	ctg	gac	ttg	cac	aag	999	940	ada		gay	Con	. 900	Clu	ttg	305
_	Ser	Leu	Asp	Leu			GIA	GIU	гга			Sei	Ald	GIU	Leu	
145					150					155					160	2022
ctg	agg	cag	tgg	gct	cag	gag	ctg	gag	, gag	aat	cto	: aat	gag	CEC	acc	1013
Leu	Arg	Gln	Trp	Ala	Gln	Glu	Leu	ı Glı			1 Lev	ı Ası	1 GIV		Thr	
				165					170					175	•	
										gccc	caat	tgtt	gcgg	ga .		1060
His	Ile	His	Gln	Ser	Leu	Lys	Ala	Gly	7							
			180					185								
agt	cago	gac	ccca	aacg	ga g	ggad	tggc	et ga	aagco	atg	g cag	gaaga	aacg	tgga	ttgtga	1120
aga	tttc	atg	gaca	ttta	tt a	gtto	ccca	aa at	taat	actt	t tta	ataai	tttc	ctat	gcctgt	1180
ctt	tacc	gca	atct	ctaa	ac a	caaa	ittgt	g a	agatt	tcat	t gga	acaci	ttat	cact	tcccca	1240
ato	aata	CCC	ttgt	gatt	tc t	tato	ccts	gt c	tta	cttta	a ato	ctcc	taat	ccts	gtcagct	1300
gag	gagg	gtg	tatg	tcac	ct c	agga	accat	tg t	gataa	attg	c gti	taac	tgca	caaa	attgtag	1360
ago	atgt	gtg	tttg	aaca	at a	tgaa	atct	tg g	gcac	cttga	a aa	aaag	aaca	ggat	caacagc	1420
aat	cgtt	cag	ggga	taag	ag a	gata	acct	tt a	aacto	ctgad	c ca	acag	tgag	ccg	ggtggag	1480
cac	gagto	ata	tttc	tttt	ct t	tcaa	aaag	ca a	atgg	gagaa	a ata	atcg	ctga	atto	tttttc	1540
tca	agcaa	agga	acat	ccct	ga c	gaaag	gaga	at g	cacc	cctg	a gg	gtgg	gtct	ata	aatggcc	1600
tco	tta	agta	taac	cato	tt c	tate	getco	ga q	actg	tagg	gat	gaaa	taaa	CCC	cagtctc	1660
															ggtcaga	1720
CCC	antte	ictc	tcaa	aacc	ct c	atct	ccta	at a	agat	atta	t ca	atqa	caat	ggt	gcctgaa	1780
201	stcat	ttag	caat	tttt	at t	tct	2000	ga t	ccta	taat	c ct	qtqa	tctc	acc	ctgcctc	1840
C21	a	5	atas	1121	ct a	atta	cctt	at a	aact	agat	g at	cttt	qtaa	CCC	acaccct	1900
															gcagctt	1960
a L 1	a	cato	2000	1220	-t '	-tos	tata	ta a	tato	toro	c to	gaca	ccta	act	ttaaaat	2020
					(	90	- J - <b>J</b>	- <u>-</u> -	-9		9	ى ـ ـ ـ ـ ـ ـ		- د ر		2036
200	cadd	aadd	aaaa	aaa												

```
<210> 46
<211> 1276
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 443..619
<221> sig_peptide
<222> 443..589
<223> Von Heijne matrix
      score 7
      seq LICVVCLYIVCRC/GS
<221> polyA_site
<222> 1267..1276
<400> 46
gaggcactca cggcatttca ttgctacttt aattttcatt attatgggat tgattgctgt
                                                                       60
cacagctact gctgcagtag ctggagttgc tttgcattcc acagtacaaa cagcagacta
                                                                      120
                                                                      180
tgtaaataat tggtagaaaa attctactct gctgtggaat taccaagata atatagacca
gaaactagct gatcaaatta atgatctcca acaaactgta atgtggctag gggatcatat
                                                                      240
                                                                      300
agttagttta gaatatagaa tgcggttaca atgtgattga aatacctctg atttttgcat
                                                                      360
tactcctcat ctgtgtaatg aaacagagca tgagtgggaa aaagttaaga gatatttaaa
                                                                      420
aggicatact agaaatttat cittggatat tgcaaagcta aaggaacaag tatticaagc
                                                                       472
coctcagata catotgacac ta atg coa gga act gaa gtg ctt gaa gga gct
                         Met Pro Gly Thr Glu Val Leu Glu Gly Ala
                                          -45
aca gac gga tta gca gct att aac ctg cta aaa tgg atc aag aca ctt
                                                                       520
Thr Asp Gly Leu Ala Ala Ile Asn Leu Leu Lys Trp Ile Lys Thr Leu
                -35
                                     -30
                                                                       568
gga ggc tct gtg att tca atg att gtg ctt tta atc tgt gtt gtt tgt
Gly Gly Ser Val Ile Ser Met Ile Val Leu Leu Ile Cys Val Val Cys
             -20
                                 -15
                                                                       616
ctt tat ata gtc tgt aga tgc gga agc cac ctc tgg aga gaa agc cac
Leu Tyr Ile Val Cys Arg Cys Gly Ser His Leu Trp Arg Glu Ser His
                                                                       669
cac tgagagcaag caatgatagc tgtggcggtt ttgcaaaaag aaaagggaga
His
10
                                                                       729
caagegeeca getatagtta ecaataaage atggtaetgg tattaaaata ggeatgtgtt
                                                                       789
ctgttccaat ggaacagaat agagaaccca gaaacaaagc caaatattta cagccaactg
                                                                       849
atctctgaca aagcaaacaa aaacataaag tggggaaagg acaccctatt ccacaaatag
                                                                       909
tgcagggata attggcaagc cacatgtaga aaaatgaagc tggatcctcg tctctcactt
tatacaaaaa tcaactcaaa atgggtcaaa gtcttaactc taagacctga aaccataaca
                                                                       969
attotagaaa ataacattgg aaaaactott ctagacattg gtttaggcaa aaagttoatg
                                                                      1029
accaagaacc caaaagcaaa tgcaataaaa aggaagataa atagatggga cctaattaag
                                                                      1089
ctgaaaagct tctgcatagc aaaaggaata atcagcagag caaacagaca acccacaggg
                                                                      1149
                                                                      1209
tgggagaaaa tatttgcaag ctatgtatct gacaatggac taatatccag aatctacaag
gaattcaaac aattagcaag aaaaaacact tgtattgtgt ttgctctgta aatcagcaaa
                                                                      1269
                                                                      1276
aaaaaaa
```

<210> 47</211> 747

<212> DNA

<213> Homo sapiens

<220> <221> CDS <222> 206..745 <400> 47 accaquagea ggtgatttcc gageteagea atgeteaget cataatgatg teaageacea tggccagttt tatgaatggc ttcctgtgtc taatgaccct gacaacccat gttcactcaa 120 gtgccaagcc aaaggaacaa ccctggttgt tgaactagca cctaaggtct tagatggtac 180 232 gcgttgctat acagaatctt tggat atg tgc atc agt ggt tta tgc caa att Met Cys Ile Ser Gly Leu Cys Gln Ile 280 gtt ggc tgc gat cac cag ctg gga agc acc gtc aag gaa gat aac tgt Val Gly Cys Asp His Gln Leu Gly Ser Thr Val Lys Glu Asp Asn Cys 15 20 10 ggg gtc tgc aac gga gat ggg tcc acc tgc cgg ctg gtc cga ggg cag 328 Gly Val Cys Asn Gly Asp Gly Ser Thr Cys Arg Leu Val Arg Gly Gln 30 35 376 tat aaa too cag oto too goa acc aaa tog gat gat act gtg gtt goa Tyr Lys Ser Gln Leu Ser Ala Thr Lys Ser Asp Asp Thr Val Val Ala 50 45 att ccc tat gga agt aga cat att cgc ctt gtc tta aaa ggt cct gat 424 Ile Pro Tyr Gly Ser Arg His Ile Arg Leu Val Leu Lys Gly Pro Asp 65 472 cac tta tat ctg gaa acc aaa acc ctc cag ggg act aaa ggt gaa aac His Leu Tyr Leu Glu Thr Lys Thr Leu Gln Gly Thr Lys Gly Glu Asn 520 agt etc age tec aca gga act tte ett gtg gac aat tet agt gtg gac Ser Leu Ser Ser Thr Gly Thr Phe Leu Val Asp Asn Ser Ser Val Asp 100 95 ttc cag aaa ttt cca gac aaa gag ata ctg aga atg gct gga cca ctc 568 Phe Gln Lys Phe Pro Asp Lys Glu Ile Leu Arg Met Ala Gly Pro Leu 115 aca gca gat ttc att gtc aag att cgt aac tcg ggc tcc gct gac agt 616 Thr Ala Asp Phe Ile Val Lys Ile Arg Asn Ser Gly Ser Ala Asp Ser 130 125 aca gtc cag ttc atc ttc tat caa ccc atc atc cac cga tgg agg gag 664 Thr Val Gln Phe Ile Phe Tyr Gln Pro Ile Ile His Arg Trp Arg Glu 150 145 712 acg gat ttc ttt cct tgc tca gca acc tgt gga gga ggt tat cag ctg Thr Asp Phe Phe Pro Cys Ser Ala Thr Cys Gly Gly Gly Tyr Gln Leu 160 155 747 aca tcg gct gag tgc tac gat ctg agg agc aac cg Thr Ser Ala Glu Cys Tyr Asp Leu Arg Ser Asn 170 175

<210> 48
<211> 561
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 36..521

<221> sig\_peptide
<222> 36..104
<223> Von Heijne matrix score 7.4

seg VLLLAALPPVLLP/GA

<221> polyA signal <222> 528..533 \ <221> polyA\_site <222> 548..561 <400> 48 gacgcctctt tcagcccggg atcgcccag caggg atg ggc gac aag atc tgg 53 Met Gly Asp Lys Ile Trp 101 Leu Pro Phe Pro Val Leu Leu Ala Ala Leu Pro Pro Val Leu Leu -10 cct ggg gcg gcc ggc ttc aca cct tcc ctc gat agc gac ttc acc ttt 149 Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu Asp Ser Asp Phe Thr Phe 5 10 197 acc ctt ccc gcc ggc cag aag gag tgc ttc tac cag ccc atg ccc ctg Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe Tyr Gln Pro Met Pro Leu 25 aag gcc tcg ctg.gag atc gag tac caa gtt tta gat gga gca gga tta 245 Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val Leu Asp Gly Ala Gly Leu 40 gat att gat ttc cat ctt gcc tct cca gaa ggc aaa acc tta'gtt ttt 293 Asp Ile Asp Phe His Leu Ala Ser Pro Glu Gly Lys Thr Leu Val Phe. 341 gaa caa aga aaa tca gat gga gtt cac act gta gag act gaa gtt ggt Glu Gln Arg Lys Ser Asp Gly Val His Thr Val Glu Thr Glu Val Gly 70 75 gat tac atg ttd tgc ttt gac aat aca ttc agc acc att tct gag aag 389 Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe Ser Thr Ile Ser Glu Lys 90 gtg att ttc ttt gaa tta atc ccg gat aat atg gga gaa cag gca caa 437 Val Ile Phe Phe Glu Leu Ile Pro Asp Asn Met Gly Glu Gln Ala Gln 105 100 gaa caa gaa gat tgg aag aaa tat att act ggc aca gat ata ttg gat 485 Glu Glu Asp Trp Lys Lys Tyr Ile Thr Gly Thr Asp Ile Leu Asp 115 120 atg aaa ctg gaa gac atc ctg gtc agt atg gtc ttc taataaaata 531 Met Lys Leu Glu Asp Ile Leu Val Ser Met Val Phe 135 561 aaaattatta acagccaaaa aaaaaaaaaa

<210> 49 <211> 632

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 36..395

<221> sig peptide

<222> 36..104

<223> Von Heijne matrix score 7.4 seq VLLLAALPPVLLP/GA

<221> polyA\_signal <222> 599..604

WO 99/31236

<221> polyA\_site <222> 619..632

<400	> 49															
gacg	cctc	tt t	cágo	ccgg	g at	.cgcc	ccag	caç	gg a	itg g let G	gc g	sp I	ag a ys I 20	itc tile I	j.rb Ga	53
										-+-	+			cta	cta	101
ctg	ccc	ttc	CCC	gtg	CTC	ctt	ctg	gcc	get	Ton	Dwa	Dea	77-1	Leu	Len	
		-15				Leu	-10					- 5				٠,
cct	ggg	gcg	gcc	ggc	ttc	aça	cct	tcc	ctc	gat	agc	gac	ttc	acc	ttt	149
Pro	Gly	Ala	Ala	Gly	Phe	Thr	Pro	Ser	Leu	Asp	Ser	Asp	Phe	Thr	Phe	
	1				5					10					15	- 07
acc	ctt	CCC	gcc	ggc	cag	aag	gag	tgc	ttc	tac	cag	ccc	atg	CCC	ctg	197
Thr	Leu	Pro	Ala	Gly	Gln	Lys	Glu	Cys		Tyr	Gln	Pro	Met	Pro	Leu	
				20					25					30		245
aag	gcc	tcg	ctg	gag	atc	gag	tac	caa	gtt	tta	gat	gga	gca	gga	tta	245
Lys	Ala	Ser	Leu	Glu	Ile	Glu	Tyr	Gln	Val	Leu	Asp	Gly	Ala	Gly	Leu	
_			35					40					45			٠,
gat	att	gat	ttc	cat	ctt	gcc	tct	cca	gaa	ggc	aaa	acc	tta	gtt	ttt	293
Asp	Ile	Asp 50	Phe	His	Leu	Ala	Ser 55	Pro	Glu	Gly	Lys	Thr 60	Leu	Val	Phe	
gaa	caa	aga	aaa	tca	qat	qqa	gtt	cac	acg	tgt	ata	aga	agt	aaa	aat	341
Glu	Gln	Arq	Lys	Ser	Asp	Gly	Val	His	Thr	Cys	Ile	Arg	Ser	Lys	Asn	
	65		•		•	70					75					
aaa	cca	qqc	act	gcg	gtt	cac	gcc	tat	aat	ccc	agc	act	ttc	cga	ggc	389
Glv	Pro	Gly	Thr	Ala	Val	His	Ala	Tyr	naA	Pro	Ser	Thr	Phe	Arg	Gly	
80					85					90					95	
caa Gln		tag	agac	tga i	agtt	ggtg	at t	acat	gttc	t gc	tttg	acaa	tac	attc	agc	445
GIII	val	a+ a	2022	aata	st t	ttct	ttga	a tt	aatc	ctaa	ata	atat	aaa	agaa	caggca	505
acci	2020	ery .	ayaa	33-3	22 7	2221	atat	t ac	taac	acad	ata	tatt	gga	tata	aaactg	565
caas	ggac	tee	aaya taat	c=4+	at o	atet	tota	a ta	-55~ aaat	aaaa	att	atta	aca	qcca	aaaaaa	625
		LCC	Lygt	cayt	at g	gict	ccca	<u>.</u>		_~~~				J = - =		632
aaaa	aaaa															

<210> 50

<211> 370

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 21..41

<221> polyA\_signal

<222> 328..333

<221> polyA\_site

attgcaaaaa aaaaaaaaa

<222> 357..370

631

```
<210> 51
<211> 994
<212> DNA
<213> Homo sapiens
<220>
<221> CDS ···
<222> 35..631
<221> sig_peptide
<222> 35..160
<223> Von Heijne matrix
      score 8.6
      seq ASLFLLLSLTVFS/IV
<221> polyA_signal
<222> 901..906 +
<221> polyA_site
<222> 979..994
<400> 51
                                                                        55
ataattggag ctgcaaagca gatcgtgaca agag atg gac ggt cag aag aaa aat
                                       Met Asp Gly Gln Lys Lys Asn
                                               -40
tgg aag gac aag gtt gtt gac ctc ctg tac tgg aga gac att aag aag
                                                                       103
Trp Lys Asp Lys Val Val Asp Leu Leu Tyr Trp Arg Asp Ile Lys Lys
-35
                     -30
                                         -25
act gga gtg gtg ttt ggt gcc agc cta ttc ctg ctg ctt tca ttg aca
                                                                       151
Thr Gly Val Val Phe Gly Ala Ser Leu Phe Leu Leu Ser Leu Thr
                 -15
                                     -10
gta ttc agc att gtg agc gta aca gcc tac att gcc ttg gcc ctg ctc
                                                                       199
Val Phe Ser Ile Val Ser Val Thr Ala Tyr Ile Ala Leu Ala Leu Leu
tct gtg acc atc agc ttt agg ata tac aag ggt gtg atc caa gct atc
                                                                       247
Ser Val Thr Ile Ser Phe Arg Ile Tyr Lys Gly Val Ile Gln Ala Ile
                         20
 cag aaa tca gat gaa ggc cac cca ttc agg gca tat ctg gaa tct gaa
                                                                       295
 Gln Lys Ser Asp Glu Gly His Pro Phe Arg Ala Tyr Leu Glu Ser Glu
                                         40
 gtt gct ata tct gag gag ttg gtt cag aag tac agt aat tct gct ctt
                                                                       343
 Val Ala Ile Ser Glu Glu Leu Val Gln Lys Tyr Ser Asn Ser Ala Leu
                                     55
                 50
 ggt cat gtg aac tgc acg ata aag gaa ctc agg cgc ctc ttc tta gtt
                                                                       391
 Gly His Val Asn Cys Thr Ile Lys Glu Leu Arg Arg Leu Phe Leu Val
                                 70
 gat gat tta gtt gat tct ctg aag ttt gca gtg ttg atg tgg gta ttt
                                                                       439
 Asp Asp Leu Val Asp Ser Leu Lys Phe Ala Val Leu Met Trp Val Phe
                             85
 acc tat gtt ggt gcc ttg ttt aat ggt ctg aca cta ctg att ttg gct
                                                                       487
 Thr Tyr Val Gly Ala Leu Phe Asn Gly Leu Thr Leu Leu Ile Leu Ala
                         100
 ctc att tca ctc ttc agt gtt cct gtt att tat gaa cgg cat cag gca
                                                                       535
 Leu Ile Ser Leu Phe Ser Val Pro Val Ile Tyr Glu Arg His Gln Ala
 110
                     115
                                          120
 cag ata gat cat tat cta gta ctt gca aat aag aat gtt aaa gat gct
                                                                       583
 Gln Ile Asp His Tyr Leu Val Leu Ala Asn Lys Asn Val Lys Asp Ala
                                      135
```

atg gct aaa atc caa gca aaa atc cct gga ttg aag cgc aaa gct gaa

Met Ala Lys Ile Gln Ala Lys Ile Pro Gly Leu Lys Arg Lys Ala Glu	
tgaaaacgcc caaaataatt agtaggagtt catctttaaa ggggatattc atttgattat acgggggagg gtcagggaag aacgaacctt gacgttgcag tgcagtttca cagatcgttg ttagatcttt atttttagcc atgcactgtt gtgaggaaaa attacctgtc ttgactgcca tgtgttcatc atcttaagta ttgtaagctg ctatgtatgg atttaaaccg taatcatatc	691 751 811 871
ttttcctat ctatctgagg cactggtgga ataaaaaacc tgtatatttt actttgttgc agatagtctt gccgcatctt ggcaagttgc agagatggtg gagctagaaa aaaaaaaac aaa	931 991 994
	•
<210> 52 <211> 412 <212> DNA <213> Homo sapiens	
<220>	,
<221> CDS <222> 271399	
<400> 52 gccgctagcg cctcgagcga tgcacctcct ttccaactgg gcaaaccccg cttccagcag	. 60
acgtecttet atggeegett caggeactte ttggatatea tegaceeteg cacactettt gteactgaga gaegteteag agaggetgtg cagetgetgg aggaetataa geatgggace	120 180
ctgcgcccgg gggtcaccaa tgaacagctc tggagtgcac agaaaatcaa gcaggctatt ctacatccgg acaccaatga gaagatcttc atg cca ttt aga atg tca ggt tat	240 294
Met Pro Phe Arg Met Ser Gly Tyr	
att cct ttt ggg acg cca att gta agt gtt acc ttc aaa gga ttt cct  Ile Pro Phe Gly Thr Pro Ile Val Ser Val Thr Phe Lys Gly Phe Pro  10 15 20	342
ttt cta aaa aat tat ttt aaa tgt cta act tta tgt tat tgc tca cgg Phe Leu Lys Asn Tyr Phe Lys Cys Leu Thr Leu Cys Tyr Cys Ser Arg 25 30 35 40	390
gta ttt gac tgaattgttg att Val Phe Asp	412
	•
<210> 53 <211> 597	
<212> DNA <213> Homo sapiens	
<220> <221> CDS	
<222> 103252	
<221> sig_peptide <222> 103213	
<223> Von Heijne matrix score 3.9 seq PGPSLRLFSGSQA/SV	
<221> polyA_site <222> 588597	
<400> 53 gaaaggtcag aggaaggagc tgtgggaagc tcgcagcagg tatcggagct taagccagtg	60
gatattggggg coctgggctc cctagccggc tgcggtgtga ga atg gag tgg gca  Met Glu Trp Ala	114

WO 99/31236 -32-PCT/IB98/02122

	Ψį.				- 3	=	
gga aag cag Gly Lys Gln	Arg Asp I	ttt cag gt Phe Gln Va	al Arg Al	a gct ccg a Ala Pro	Gly Trp F	at cat Asp His	162
	-30		-25		-20	at 636	210
ttg gcc tcc Leu Ala Ser -15		Gly Pro Se					210
gcg agt gtc	tot act (			t aga act	-		252
Ala Ser Val	Cys Ser						
tgatgtcatg	1	-	at tagct		gggaaa ca	agccaattt	312
tcttgacttt	_	-					372
ctctaaaaag							432
gaatcttta							492
agggaaactc							552
ctcttggtgc							597
•							
							•
				•			
<210> 54	•	•					
<211> 748	•						•
<212> DNA	_			•	1		
<213> Homo	sapiens	• •					
<220>							
<221> CDS							
<222> 246	0			· •			
<221> polyA	_					•	
<222> 713	718						
	1.						
<221> polyA	_site	,					
	_site						
<221> polyA <222> 735	_site 748						
<221> polyA <222> 735 <400> 54 c aca gtt c	_site 748 ct ctc ct						49
<221> polyA <222> 735 <400> 54 c aca gtt c Thr Val P	_site 748 ct ctc ct ro Leu Le			Asp His A		y Arg Ala	49
<221> polyA <222> 735 <400> 54 c aca gtt c Thr Val P	_site 748 ct ctc ct ro Leu Le 5	u Leu Glu	Pro Ala	Asp His A	la Arg Gl	y Arg Ala 15	
<221> polyA <222> 735 <400> 54 c aca gtt c Thr Val P 1 cat gtc cac	_site 748 ct ctc ct ro Leu Le 5 cta cct	u Leu Glu gaa aat g	Pro Ala tt cgc a	Asp His A 10 gc cag tct	la Arg Gl cct ggc	y Arg Ala 15 cat gtg	49 97
<221> polyA <222> 735 <400> 54 c aca gtt c Thr Val P	_site 748 ct ctc ct ro Leu Le 5 cta cct Leu Pro	u Leu Glu gaa aat g	Pro Ala tt cgc a al Arg S	Asp His A 10 gc cag tct	cct ggc Pro Gly	y Arg Ala 15 cat gtg	
<221> polyA <222> 735 <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His	_site 748 ct ctc ct ro Leu Le 5 cta cct Leu Pro 20	u Leu Glu gaa aat g Glu Asn V	Pro Ala tt cgc a al Arg S 25	Asp His A 10 gc cag tct er Gln Ser	la Arg Gl cct ggc Pro Gly 30	y Arg Ala 15 cat gtg His Val	97
<221> polyA <222> 735 <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His	_site 748 ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt	u Leu Glu gaa aat g Glu Asn V ggt gca c	Pro Ala tt cgc a al Arg S 25 ag gta c	Asp His A 10 gc cag tct er Gln Ser ta ccg acc	la Arg Gl cct ggc Pro Gly 30 gga cct	y Arg Ala 15 cat gtg His Val gat gag	
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val F 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly	_site 748 ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt	gaa aat g Glu Asn V ggt gca c Gly Ala G	Pro Ala tt cgc a al Arg S 25 ag gta c ln Val L	Asp His A 10 gc cag tct er Gln Ser ta ccg acc	cct ggc Pro Gly 30 gga cct Gly Pro	y Arg Ala 15 cat gtg His Val gat gag	97
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35	_site 748 ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt Arg Ser	gaa aat g Glu Asn V ggt gca c Gly Ala G	Pro Ala tt cgc a al Arg S 25 ag gta c ln Val L	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr	cct ggc Pro Gly 30 gga cct Gly Pro 45	y Arg Ala 15 cat gtg His Val gat gag Asp Glu	97 145
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt	_site 748  ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt Arg Ser	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g	Pro Ala tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr	cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta	97
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val	_site 748  ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt Arg Ser	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V	Pro Ala tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag	cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta	97 145
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50	_site 748  ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt Arg Ser gag aag Glu Lys	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V	Pro Ala tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60	cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu	97 145 193
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga	_site 748  ct ctc ct ro Leu Le	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a	Pro Ala tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act	97 145
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg	_site 748  ct ctc ct ro Leu Le	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu I	Pro Ala tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr	97 145 193
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65	_site 748  ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt Arg Ser gag aag Glu Lys ttt gag Phe Glu	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu I 70	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80	97 145 193
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65 gga tca cas	_site 748  ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt Arg Ser gag aag Glu Lys ttt gag The Glu	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu 1 70 cgg tcg g	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75	cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg	97 145 193
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65	_site 748  ct ctc ct ro Leu Le	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu 1 70 cgg tcg g	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L ag aac t lu Asn T	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75 cgg aag gtc	cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg Glu Ser	97 145 193
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65 gga tca caa Gly Ser Glr	_site 748  ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt Arg Ser gag aag Glu Lys ttt gag Phe Glu gtc ttt Val Phe 85	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu L 70 cgg tcg g Arg Ser G	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L ag aac t lu Asn T	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75 cgg aag gtc	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca Trp Ala	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg Glu Ser 95	97 145 193
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65 gga tca caa Gly Ser Glr agc aga gga	_site 748  ct ctc ct ro Leu Le	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu I 70 cgg tcg g Arg Ser G	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L ag aac t lu Asn T ggc cta g	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75 gg aag gtc crp Lys Val 00 gac ttg tgc	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca Trp Ala	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg Glu Ser 95 ctg tgt	97 145 193 241 289
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65 gga tca caa Gly Ser Glr	_site 748  ct ctc ct ro Leu Le	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu I 70 cgg tcg g Arg Ser G	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L ag aac t lu Asn T ggc cta g	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75 gg aag gtc crp Lys Val 00 gac ttg tgc	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca Trp Ala	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg Glu Ser 95 ctg tgt	97 145 193 241 289
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65 gga tca caa Gly Ser Glr agc aga gga Ser Arg Gly	_site 748  ct ctc ct ro Leu Le	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu L 70 cgg tcg g Arg Ser G	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L ag aac t lu Asn T cgc cta g cys Leu A	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75 gg aag gtc crp Lys Val 00 gac ttg tgc	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca Trp Ala tca gtg Ser Val 110	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg Glu Ser 95 ctg tgt Leu Cys	97 145 193 241 289
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65 gga tca caa Gly Ser Glr agc aga gga ser Arg Gly tgg gga gaa	_site 748  ct ctc ct ro Leu Le	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu L 70 cgg tcg g Arg Ser G	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L ag aac t clu Asn T cgc cta g cys Leu A 105 ata cct g	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75 gg aag gtc crp Lys Val 00 gac ttg tgc asp Leu Cys	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca Trp Ala tca gtg ser Val 110 cca aag	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg Glu Ser 95 ctg tgt Leu Cys cgt gga	97 145 193 241 289
<221> polyA <222> 735  <400> 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly 35 aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65 gga tca caa Gly Ser Glr agc aga gga Ser Arg Gly	_site 748  ct ctc ct ro Leu Le	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu L 70 cgg tcg g Arg Ser G gat gac t Asp Asp C cgg aca a Arg Thr I	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L ag aac t clu Asn T cgc cta g cys Leu A 105 ata cct g	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75 gg aag gtc crp Lys Val 00 gac ttg tgc asp Leu Cys	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca Trp Ala tca gtg ser Val 110 cca aag	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg Glu Ser 95 ctg tgt Leu Cys cgt gga	97 145 193 241 289
<pre>&lt;221&gt; polyA &lt;222&gt; 735 &lt;400&gt; 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65 gga tca caa Gly Ser Glr agc aga gga Ser Arg Gly tgg gga gaa Trp Gly Glv 115</pre>	_site 748  ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt Arg Ser gag aag Glu Lys ttt gag Phe Glu gtc ttt Val Phe 85 gac cat Asp His 100 actg cta Leu Leu 6	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu L 70 cgg tcg g Arg Ser G gat gac t Asp Asp C cgg aca a Arg Thr I	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L ag aac t lu Asn T gc cta g cys Leu A 105 tta cct g lta cct g	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75 gg aag gtc crp Lys Val color ttg tgc gac att cca gaa att cca silu Ile Pro	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca Trp Ala tca gtg Ser Val 110 cca aag Pro Lys 125	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg Glu Ser 95 ctg tgt Leu Cys cgt gga Arg Gly	97 145 193 241 289
<pre>&lt;221&gt; polyA &lt;222&gt; 735 &lt;400&gt; 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65 gga tca caa Gly Ser Glr agc aga gga Ser Arg Gly tgg gga gaa Trp Gly Glu gaa ctc aaa</pre>	_site 748  ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt Arg Ser gag aag Glu Lys ttt gag Phe Glu gtc ttt Val Phe 85 gac cat Asp His 100 ctg cta Leu Leu acg gag	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu I 70 cgg tcg g Arg ser G gat gac t Asp Asp C cgg aca a Arg Thr I ctt ttg S	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L ag aac t lu Asn T gc cta g cys Leu A lo ct gat lo cot gat	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75 gg aag gtc rp Lys Val oct ttg tgc gac att cca gaa att cca aag aa gaa aga	la Arg Gl cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca Trp Ala tca gtg Ser Val 110 cca aag Pro Lys 125 aaa cac	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg Glu Ser 95 ctg tgt Leu Cys cgt gga Arg Gly aaa cct	97 145 193 241 289 337
<pre>&lt;221&gt; polyA &lt;222&gt; 735 &lt;400&gt; 54 c aca gtt c Thr Val P 1 cat gtc cac His Val His  cgc agg ggc Arg Arg Gly aaa cag gtt Lys Gln Val 50 gtg aga cga Val Arg Arg 65 gga tca caa Gly Ser Glr agc aga gga Ser Arg Gly tgg gga gaa Trp Gly Glv 115</pre>	_site 748  ct ctc ct ro Leu Le 5 cta cct Leu Pro 20 aga agt Arg Ser gag aag Glu Lys ttt gag Phe Glu gtc ttt Val Phe 85 gac cat Asp His 100 ctg cta Leu Leu acg gag	gaa aat g Glu Asn V ggt gca c Gly Ala G agt gaa g Ser Glu V 55 gat ctg a Asp Leu I 70 cgg tcg g Arg ser G gat gac t Asp Asp C cgg aca a Arg Thr I ctt ttg S	Pro Ala  tt cgc a al Arg S 25 ag gta c ln Val L 0 tt gat t al Asp P ag ccc a ys Pro L ag aac t lu Asn T gc cta g cys Leu A lo ct gat lo cot gat	Asp His A 10 gc cag tct er Gln Ser ta ccg acc eu Pro Thr tc tca aag he Ser Lys 60 ag ctt tct ys Leu Ser 75 gg aag gtc rp Lys Val oct ttg tgc gac att cca gaa att cca aag aa gaa aga	la Arg Gl  cct ggc Pro Gly 30 gga cct Gly Pro 45 tca cat Ser His gtt tgc Val Cys tgg gca Trp Ala tca gtg Ser Val 110 cca aag Pro Lys 125 aaaa cac Lys His	y Arg Ala 15 cat gtg His Val gat gag Asp Glu agc tta Ser Leu aaa act Lys Thr 80 gag tcg Glu Ser 95 ctg tgt Leu Cys cgt gga Arg Gly aaa cct	97 145 193 241 289 337

480 .

• •	
caa gtt tot caa cag gag gaa ott aaa taactatgoo aagaattotg	480
Gln Val Ser Gln Glu Glu Leu Lys	
150	
143 and another and the state of the state o	540
totastocts actorsadad daddtoctod quyangura	600
	660
aaccatttca tgaatatggt ttggaagatg tttagtcttg aatataatgc gaaatagaat	720
atttgtaagt ctaccaaaaa aaaaaaaa	748
attiglaage couldurate same	•
<210> 55	
<211> 703	
<212> DNA	
<213> Homo sapiens	
•	•
<220>	
<221> CDS	
<222> 31231	
<221> polyA_signal	
<222> 769774	•
<221> polyA_site	
<222> 690703	
<400> 55	54
ctctggtggc tctgctacgg cggcgcagaa atg agg cag aag cgg aaa gga gat Met Arg Gln Lys Arg Lys Gly Asp	
net Arg Gin 1/5 125 274 287 1	
ctc agc cct gct aag ctg atg atg ctg act ata gga gat gtt att aaa	102
Leu Ser Pro Ala Lys Leu Met Met Leu Thr Ile Gly Asp Val Ile Lys	
caa ctg att gaa gcc cac gag cag ggg aaa gac atc gat cta aat aag	150
caa ctg att gaa gee tae gag tag ggg dad gab lee Asp Lee Asn Lys Gln Leu Ile Glu Ala His Glu Gln Gly Lys Asp Ile Asp Leu Asn Lys	
• • • • • • • • • • • • • • • • • • • •	
gtg aga acc aag aca gct gcc aaa tat ggc ctt tct gcc cag ccc cgc	198
gtg aga acc aag ata get get daa tut ggb beu Ser Ala Gln Pro Arg Val Arg Thr Lys Thr Ala Ala Lys Tyr Gly Leu Ser Ala Gln Pro Arg	
Val Arg Thr Lys Int Ala Ala Liys 171 Car 200 55	•
ctg gtg gat atc att gct gcc gtc cct cct gag tagctgggat tacaggcacc	251
Leu Val Asp Ile Ile Ala Ala Val Pro Pro Glu	
Leu Val Asp lie lie Ala Ala Val 120 120 000	
and a state of a state of a grant good to the state of th	311
	371
accommon conference attention of the conference of the confe	431
	491
at at a contract of a contract the contract of	551
	611
actitiggaga citigategg agustaaaq qaattqattc ctctgaaagg gcctgaaaat	611 671
gctcctgtgg cattttacaa aggtttaaag gaattgatte ctttgaaagg goodgaaag	611
gctcctgtgg cattttacaa aggtttaaag gaattgattc ctctgaaagg gcctgaaaat aaaaaagtctt taacatacaa aaaaaaaaa aa	611 671

<210> 56 <211> 725 <212> DNA

<213> Homo sapiens

<220> <221> CDS <222> 305..565 <221> polyA signal <222> 694..699 ' <221> polyA\_site <222> 713..725 <400> 56 ctcacggtgg tgaaggtcac agggttgcag cactcccagt agaccaggag ctccgggagg 60 cagggeegge eccaegteet etgegeacea ecctgagttg gateetetgt gegeeaceee 120 tgagttggat ccagggctag ctgctgttga cctccccact cccacgctgc cctcctgcct 180 grageratga egecectget careetgate etggtggtee teatgggett acetetggee 240 caggecttgg actgccacgt gtgaggacta caaatecete caggatatea ttgccateet 300 gggt atg gat gaa ctt tot gag gaa gac aag ttg acc gtg too cgt gca 349 Met Asp Glu Leu Ser Glu Glu Asp Lys Leu Thr Val Ser Arg Ala 10 397 cgg aaa ata cag cgt ttc ttg tct cag cca ttc cag gtt gct gag gtc Arg Lys Ile Gln Arg Phe Leu Ser Gln Pro Phe Gln Val Ala Glu Val 20 445 tte aca ggt cat atg ggg aag etg gta eee etg aag gag ace ate aaa Phe Thr Gly His, Met Gly Lys Leu Val Pro Leu Lys Glu Thr Ile Lys 40 493 gga ttc cag cag att ttg gca ggt gaa tat gac cat ctc cca gaa cag Gly Phe Gln Gln Ile Leu Ala Gly Glu Tyr Asp His Leu Pro Glu Gln 55 gcc ttc tat atg gtg gga ccc att gaa gaa gct gtg gca aaa gct gat 541 Ala Phe Tyr Met Val Gly Pro Ile Glu Glu Ala Val Ala Lys Ala Asp 75 70 aag ctg gct gaa gag cat tca tcg tgaggggtct ttgtcctctg tactgtctct 595 Lys Leu Ala Glu Glu His Ser Ser ctccttgccc ctaacccaaa aagcttcatt tttctgtgta ggctgcacaa gagccttgat 655 tgaagatata ttctttctga acagtattta aggtttccaa taaagtgtac acccctcaaa 715 725 aaaaaaaaa <210> 57 <211> 1705 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 124..873 <221> sig\_peptide <222> 124..378 <223> Von Heijne matrix score 3.6 seq HLSVVTLAAKVKC/IP <221> polyA signal <222> 1673..1678 <221> polyA\_site <222> 1694..1705 <400> 57 cggaggtgag gagcggcggc cccgcccggt gcgctggagg tcgaagcttc caggtagcgg 60

cccgcagagc ctgacccagg ctctggacat cctgagccca agtcccccac actcagtgca gtg atg agt gcg gaa gtg aag gtg aca ggg cag aac cag gag caa ttt

Met Ser Ala Glu Val Lys Val Thr Gly Gln Asn Gln Glu Gln Phe

120

						0.0					-75					
	-85		acc	220	tca	-80	aag	aaa	aca	aca		qcc	aca	ctc	atc	216
CEG	T.e.	Cca Len	Ala	Lvs	Ser	Ala	Lys	Gly	Ala	Ala	Leu	Ala	Thr	Leu -	Ile	•-
-70					-65					-60					- 55	264
cat	cag	gtg	ctġ	gag	gcc	cct	ggt	gtc	tac	gtg	ttt	gga	gaa	ctg	ctg	264
His	Gln	Val	Leu	Glu	Ala	Pro	Gly	Val	Tyr	Val	Phe	Gly	Glu	_40	Leu	
				-50					-45			-++	act	-	cta	312
gac	atg	CCC	aat	gtt	aga	gag	ctg	naa	gcc	cgg	aat Acn	Ten	cct	Pro	Leu	
Asp	Met	Pro		Val	Arg	GIU	ren	-30	Ald	Arg	Man	БСи	Pro			•
			-35	224	a a t	220	ctt		cac	ctc	tca	att	gtc	acc	ctg	360
aca	gag	y) a	Gln	Lvs	Δen	Lvs	Leu	Ara	His	Leu	Ser	val	Val	Thr	Leu	
		-20					-15					-10				
act	act	222	ata	aag	tgt	atc	cca	tat	gca	gtg	ttg	ctg	gag	gct	ctt	408
Ala	Ala	Lys	Val	Lys	Cys	Ile	Pro	Tyr	Ala	Val	Leu	Leu	Glu	Ala	Ten	
	-5					1				5					10	456
gcc	ctg	cgt	aat	gtg	cgg	cag	ctg	gaa	gac	CTT	gtg	att	gag	Ala	Val	150
Ala	Leu	Arg	Asn		Arg	GIn	Leu	GIU	Asp 20	ьеu	vaı	110	Glu	25	·	•
				15	-a+	~~~	+ c c	cta		cag	cac	aac	cag		ctc	504
tat	gct	gac	grg	T.em	Ara	Glv	Ser	Leu	Asp	Gln	Arq	Asn	Gln	Arg	Leu	
Tyr	Ala	Asp	30	שטע	9	CL		35			Ī		40			
gag	att	gac	tac	aqc	atc	ggg	cgg	gac	atc	cag	cgc	cag	gac	ctc	agt	552
Glu	Val	Asp	Tyr	Ser	Ile	Gly	Arg	Asp	Ile	Gln	Arg	GIR	Asp	Leu	Ser	
		45					50					55				600
gcc	att	gcc	cga	acc	ctg	cag	gaa	tgg	tgt	gtg	ggo	tgt	gag	gro	gtg	600
Ala		Ala	Arg	Thr	Lev		Glu	Trp	Cys	val	70	Cys	Giu	VAI	. Val	
	60		- 4-4-			65			cat			caa	cac	aac	qaq	648
ctg	tca	ggc	מכנ	gag	gag	Cay	Val	Ser	Arc	. gcc . Ala	Ası	a Glr	n His	Lys	gag Glu	
леч 75	Sei	GIY	110	GIU	80	. 021				85					90	
	cac	cta	aac	cto		cag	cag	att	gag	gagt	gag	g gt1	gcc	aac	ctt	696
Glr	Glr	Leu	Gly	Let	ı Lys	Glr	Glr	ılle	e Glu	ı Ser	Gli	u Va.	l Ala	ASI	1 Dea	
				95					100	)				10:	•	744
aaa	a aaa	acc	att	aaa	gt	ace	ace	gca	a gca	a gca	gc	c gc	a gcc	ace Th	a tct r Ser	122
Lys	Lys	Thr			s Va.	LThi	Th	C Ali	r S Ale	a Ala	A MI	d Al	120	1 111. )	r Ser	
			110	)		- at/	1	11!		a ag	д да	a cc			t ggc	792
cag	g gad	Dro	. gaç	, Cae	n Hi	s Ten	ı Th	r Gl	u Le	u Are	g Gl	u Pr	o Ala	Pr	o Gly	
		125	:				13	0				13	5			
ace	c aac	Cac	ca	ca	g cc	c age	c aa	g aa	a gc	c tc	a aa	g gg	c aag	99	g ctc v Leu	840
Th:	r Ası	ı Gli	a Arg	g G1:	n Pr	o Se	r Ly	s Ly	s Al	a Se	т ру	5 61	y Ly	s Gl	y Leu	
	14	מ				14	5				15	U				893
cg	a gg	g ag	gc	c aa	g at	t tg	g tc	c aa	g tc	g aa	t tg -	aaag	aact	gtc	gtttcct	
		y Se:	r Ala	а Lу	s Il	e Tr	p se	т ьу	s se	1 AS	11 5					
15	5				16	u aast	acct	ac c	tacc			agto	ctca	qaq	agcette	953
CC	ctgg	ggat	grg	gggt aact	gat	agtt	ctaq	at t	cato	accc	t to	acct	cccc	taa	ccccaaa	1013
ca	taga	tcac	acc	ttct	cta	aaaa	qqaq	tc a	laatg	rtagg	t Ca	atgtt	tttg	רנט	gcactt	1073
ct	attt	ttta	tga	cttc	atq	tatt	ccat	tg c	ctccc	cgct	.g co	catgo	CCCC	LUC	cergere	1133
~	ttaa	gage	t.ca	gcat	cta	tccc	tatt	.ca t	taca	itgtc	a tt	:gagt	aggu	995	glagecee	1193
Ca	taga	aatc	act	ctat	cta	gage	ataa	CC C	cacac	gcgt	יל דו	CCCC	gcca	CCC	Cattet	1253 1313
ac	atac	ctga	tcc	ccaq	ttc	ctat	acco	ta c	ccct	gaco	c a	ccgag	gcago		Lyaagag	1313
	atao	aacc	ccc	acct	tta	ctca	caco	ct g	gagaa	attct	:g g	gagc	cagic	: Lgc	catgeta	1433
99	gagto	actg	gac	atgt	tca	tcct	agaa	itc (	tgt	acac	:c a	age	-alll	. CC	ttcctct	1493
ct	ctgg	ccct	tgg	gtcc	tgg	gaat	gcts	JCT S	40 L L (	aacc	יר מי	accs.	tetee	. 20	atggcagc aagcttga	1553
CC	tttc	tcaa	cat	gttg	,aga	gate	,a(		tata	agtti	10 0.	taaa	qaaqq	g ga	aagcttga agggtata	1613
Ę	gcaa	eret	te:	12225	1222	aado	itat	ata 1	tgcai	tata	to t	atat	ataat	at	gacgcaga	1673
22	ataas	teta	taa	gaaa	atcc	aaaa	aaaa	aaa a	aa							1705
46			-5-													

```
<210> 58
<211> 1069
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 135..206
<221> polyA_signal
<222> 850..855
<221> polyA_site
<222> 1056..1069
<400> 58
cccactccgc tctcacgact aagctctcac gattaaggca cgcctgcctc gattgtccag
                                                                        60
cctctgccag aagaaagctt agcagccagc gcctcagtag agacctaagg gcgctgaatg
                                                                       120
                                                                       170
agtgggaaag ggaa atg ccg acc aat tgc gct gcg gcg ggc tgt gcc act
                Met Pro Thr Asn Cys Ala Ala Ala Gly Cys Ala Thr
                                                                       216
acc tac aac aag cac att aac atc agc ttc cac agg taacctgggc
Thr Tyr Asn Lys His Ile Asn Ile Ser Phe His Arg
                             20
agggagtggg ggtgacggaa actggagttc ctattgtggc tatcgcttgt gtggaaggaa
                                                                       276
                                                                       336
caggaggatt ctgctaattc taataacttt cccagctggt agcagggaag catcgtatgt
                                                                       396
cctttgtgtt tctcaaatct gcccaattgt tctctgcttt cggggaagct ttactcattt
                                                                       456
tctaaaaqaa atccaaqtac tgtttggtca ttacccctta gtaaaaaaaa gtaacaggag
                                                                       516
gatatcgtaa ttttctactg ttttattcct ctgttagacc gggccttgac atgaatgacg
                                                                       576
ccgtaaggga gaaagagatc ttcccaatca gcaatcaccg taaaagcctg ctgtgttccc
                                                                       636
gttaaaatta ggaaattoto actagatgaa ttgacatggg aggcatttag atttotaata
gtcacatagt aattctgcgg aggaattgag tcatctttga tagccatgga attaagcgat
                                                                       696
                                                                       756
gttaattaaa gtgcaaacga taacctttct gttcttacta gaatagagta ataaaaagaa
cctaggtttt cttttgtttg ctggaagaaa aatcaaaatt ctttagttct gtcaaaccag
                                                                       816
                                                                       876
aactettgaa agcaetttga acaatgeetg gaaaataaca ggtaetetgt aaatgtttae
                                                                       936
cttctctgca agtgcctgcc acgtgcccga agaaaagaca cattaaaaag ttaagtgaca
                                                                       996
ccagtcctga ttttatatat tttatatacc taacaacgta tatgttagta tgtagaaatt
atatecttga cetttttece tacetattae gaactgtaet tttattaaaa getgecaeta
                                                                      1056
                                                                      1069
aaaaaaaaa aaa
 <210> 59
 <211> 1084
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> CDS
 <222> 135..818
 <221> polyA signal
 <222> 909..914
 <221> polyA_site
 <222> 1071..1084
 <400> 59
                                                                         60
 cccacteege teteacgaet aageteteac gattaaggea egeetgeete gattgteeag
```

cctctgccag aagaaagctt agcagccagc gcctcagtag aggcctaagg gcgctgaatg

agtgggaaag ggaa atg ccg acc aat tgc gct gcg gcg ggc tgt gcc act

120

			<b>5.</b>	1				5				Gly	10			
acc	tac	aac	aaq.	cac	att	aac	atc	agc	ttc	cac	agg	ttt	cct	ttg	.gat	218
Thr	Tvr	Asn	Lvs	His	Ile	Asn	Ile	Ser	Phe	His	Arg	Phe	Pro	Leu	Asp	
1111	-1-	15	-7-				20				_	25				
			202	222	a a	taa		cac	cta	att	agg	cgc	aaa	aat	ttt	266
CCL	ada	aya	200	1	924	T	77-1	720	Leu	77 = 1	722	Arg	Lvs	Asp	Phe	
Pro	-	AIG	AIG	nyp	GIU		vai	Arg	neu	vai	40	9	_,_			
	30					35						+++	<b>722</b>	acc	tcc	314
gtg	cca	gga	aaa	cac	act	בננ	CLL	tgt	CCa	aay	uac mac	ttt	922	אפט	Cor	<b>7</b> ,
Val	Pro	Gly	Lys	His		Phe	Leu	Cys	Ser		HIS	Phe	GIU	AIG	60	
45			11.		50					55						262
tgt	ttt	gac	cta	aca	gga	caa	act	cga	cga	ctt	aaa	atg	gat	gct	gcc	362
Cys	Phe	Asp	Leu	Thr	Gly	Gln	Thr	Arg		Leu	Lys	Met	Asp		vaı	
				65					70					75		
cca	acc	att	ttt	gat	ttt	tgt	acc	cat	ata	aag	tct	atg	aaa	ctc	aag	410
Pro	Thr	Ile	Phe	Asp	Phe	Cys	Thr	His	Ile	Lys	Ser	Met	Lys	Leu	Lys ·	
			80	_		-		85					90			•
t.ca	agg	aat	ctt	ttg	aag	aaa	aac	aac	agt	tgt	tct	cca	gct	gga	cca	458
Ser	Ara	Asn	Leu	Leu	Lys	Lys	Asn	Asn	Ser	Cys	Ser	Pro	Ala	Gly	Pro	
200	5	95			•	•	100			-		105				
tet	agt		aaa	tca	aac	att	agt	aqt	caq	caa	qta	cta	ctt	gaa	cac	506
Ser	Ser	Len	Lvs	Ser	Asn	Ile	Ser	Ser	Gln	Ġln	Val	Leu	Leu	Glu	His	
361	110	Deu	_, _			115					120					•
		~~~	+++	200	aat		ato	gag	gca	aaa.		agg	atc	att	aaa	554
age	m	772	Dhe	723	Acn	Dro	Met	Glu	Ala	Lvs	Lvs	Arg	Ile	Ile	Lvs	
	IÀI	MIG	PIIC	Arg	130	710	1400	014	7,14	135		9			140	
125							++-		200				act	tac		602
ctg	gaa	aaa	gaa	ata	gca	age	Tou	aya X	aya	Tare	acy Met	aaa	Thr	Cve	Len	**-
Leu	GIU	гÀг	GIU		WIS	Ser	beu	Ary			Met	Lys	1111	155		
				145					150			~~~				650
caa	aag	gaa	cgc	. aga	gca	act	cga	aga	tgg	atc	aaa	900	Mak	Cy C	ttg	050
Gln	Lys	Glu			Ala	Thr	Arg			TTE	гу	Ala			Leu	
			160					165					170			600
gta	aag	aat	tta	gaa	gca	aat	agt	gta	tta	cct	aaa	ggt	aca	tca	gaa	698
Val	Lys	Asn	Leu	Glu	Ala	Asn			Leu	Pro	Lys			Ser	Glu	
		175					180					185				246
cac	atg	tta	cca	act	gcc	tta	ago	agt	ctt	cct	tte	gaa	gat	ttt	aag	746
His	Met	Leu	Pro	Thr	Ala	Leu	Ser	Ser	: Lev	Pro	Lev	ı Glu	Asp	Phe	: Lys	
	190					195					200					
atc	ctt	gaa	caa	gat	caa	caa	gat	aaa	aca	cto	cta	a agt	cta	aat	cta	794
Ile	Leu	Glu	Gln	Asp	Gln	Glr	Asp	Lys	Thr	Let	Lev	ı Ser	Let	ı Ası	ı Leu	
205				-	210					215					220	
		acc	aaq	aqt	acc	tto	att	taa	attt	agc	ttg	cacag	gag d	ttga	atgcct	848
Lvs	Glr	Thr	Lys	Ser	Thr	Phe	: Ile	2			-					
-, -			<u></u>	225		_ 554										
2+4	cttc	-a++	cttt			taaa	gata	a ti	ato	cact	tai	tacca	aaaa	ttca	attattt	908
22+	2227	1+++	tact	taas	at =	acat	tact	g a	attte	taa	a da	ctta	atta	caaa	aagaata	968
aal		+	+=+-	.cyac	++ +	+=++	+ (72	ים כי	geat	- 2 ~ ·	ם מרני - שמי	aceti	aca	ttac	gaattac	1028
448	adCl	.cca	2+++	+				14 M	-545	-2200	- set	aaaaa	2222	aaaa	aaa	1084
998	CCCC	aadd	alli	. cgct	.aa l	.aaal	9-5	, - 9	y	25	, -a,					

<210> 60

<211> 419

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 33..290

<221> sig\_peptide

<222> 33..92

<223> Von Heijne matrix
score 5.4
seq WFVHSSALGLVLA/PP

<400> 60 aatggtaggc cttcatgtga gccagttact ac atg aat ctt cat ttc cca cag 53 Met Asn Leu His Phe Pro Gln -20 101 tgg ttt gtt cat tca tca gcg tta ggc ttg gtc ctg gct cca cct ttc Trp Phe Val His Ser Ser Ala Leu Gly Leu Val Leu Ala Pro Pro Phe -5 -10 . 149 tcc tct ccg ggc act gac ccc acc ttt ccg tgt att tac tgt agg cta Ser Ser Pro Gly Thr Asp Pro Thr Phe Pro Cys Ile Tyr Cys Arg Leu 10 tta aat atg atc atg acc cgc ctt gca ttt tca ttc atc acc tgt tta 197 Leu Asn Met Ile Met Thr Arg Leu Ala Phe Ser Phe Ile Thr Cys Leu 25 30 tgc cca aat tta aag gaa gtt tgt ctc att ttg cca gaa aaa aat tgt 245 Cys Pro Asn Leu Lys Glu Val Cys Leu Ile Leu Pro Glu Lys Asn Cys .,40 . 45 290 aat agt cgg cac gct gga ttt gta ggg cca gca aaa ttg cgg cag Asn Ser Arg His Ala Gly Phe Val Gly Pro Ala Lys Leu Arg Gln 55 65 " 60 tgaaactagt ttcacttcta aagcccttca tttcccacaa ggttaagctc tcgaaacccc 350 attigateet tggtteetat tiegateete etitggaate tgaaaategg tetecatgit 410 419 gtatgcaaa

<210> 61

<211> 682

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 485..616

<221> polyA site

<222> 669..682

<400> 61

60 ctcctttctc attccttatc ttgcgtgttt ttaccttttt ttcataacta agtttttgag gaagttagtg ttcttttcaa agaaccggtt cgaaatgtac ttttctttgc tactttttgt 120 tattttattg atcacatctt taatcttttg ttctctatac gtggcctgtt ttgatttatt 180 ttactattct tgctttctaa ggtaagtatt ttgttgtgta gtgctttatt tttttcatct 240 300 ttettettga ataataatga catttttagg ttataaattt teetetggta eteagtttge ctcattaatt ttggcagtaa gcattctcct tttattgctt tctatgtagt ctttaatttt 360 gcttttaact tcttctttga tctaaggatt acctacttgt taatttccaa atattatctt 420 480 gget atg teg eeg agg etg gag tge agt ggt gea ate ttg get eac tge 529 Met Ser Pro Arg Leu Glu Cys Ser Gly Ala Ile Leu Ala His Cys 10 aac ccc cgc ctc cca ggt tca agt tat tct cct gcc tca gct act tgg 577 Asn Pro Arg Leu Pro Gly Ser Ser Tyr Ser Pro Ala Ser Ala Thr Trp 25 20 gtg aga gga tcc ctt gag ccg ggg agg ttg agg ctg cag tgagccataa 626 Val Arg Gly Ser Leu Glu Pro Gly Arg Leu Arg Leu Gln 40

ccactactct ccagcctgga taacaaaagt gagactctga ccaaaaaaaa aaaaaa

680

<210> 62 <211> 1191 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 54..995 <221> sig\_peptide <222> 54..227 <223> Von Heijne matrix score 4.1 seq LVHHCPTWQWATG/EE <221> polyA signal <222> 1130..1135 <221> polyA\_site <222> 1181..1191 <400> 62 56 cacggctgca ctttccatcc cgtcgcgggg ccggccgcta ctccggcccc agg atg 104 cag aat gtg att aat act gtg aag gga aag gca ctg gaa gtg gct gag Gln Asn Val Ile Asn Thr Val Lys Gly Lys Ala Leu Glu Val Ala Glu -50 -55 tac ctg acc ccg gtc ctc aag gaa tca aag ttt agg gaa aca ggt gta 152 Tyr Leu Thr Pro Val Leu Lys Glu Ser Lys Phe Arg Glu Thr Gly Val -30 -35 att acc cca gaa gag ttt gtg gca gct gga gat cac cta gtc cac cac 200 Ile Thr Pro Glu Glu Phe Val Ala Ala Gly Asp His Leu Val His His -15 -20 -25 tgt cca aca tgg caa tgg gct aca ggg gaa gaa ttg aaa gtg aag gca 248 Cys Pro Thr Trp Gln Trp Ala Thr Gly Glu Glu Leu Lys Val Lys Ala -5 296 tac cta cca aca ggc aaa caa ttt ttg gta acc aaa aat gtg ccg tgc Tyr Leu Pro Thr Gly Lys Gln Phe Leu Val Thr Lys Asn Val Pro Cys tat aag cgg tgc aaa cag atg gaa tat tca gat gaa ttg gaa gct atc 344 Tyr Lys Arg Cys Lys Gln Met Glu Tyr Ser Asp Glu Leu Glu Ala Ile 30 392 att gaa gaa gat gat ggt gat ggc gga tgg gta gat aca tat cac aac Ile Glu Glu Asp Asp Gly Asp Gly Gly Trp Val Asp Thr Tyr His Asn 50 45 40 440 aca ggt att aca gga ata acg gaa gcc gtt aaa gag atc aca ctg gaa Thr Gly Ile Thr Gly Ile Thr Glu Ala Val Lys Glu Ile Thr Leu Glu 488 aat aag gac aat ata agg ctt caa gat tgc tca gca cta tgt gaa gag Asn Lys Asp Asn Ile Arg Leu Gln Asp Cys Ser Ala Leu Cys Glu Glu 80 75 gaa gaa gat gaa gaa gga gaa gct gca gat atg gaa gaa tat gaa 536 Glu Glu Asp Glu Asp Glu Gly Glu Ala Ala Asp Met Glu Glu Tyr Glu 95 584 gag agt gga ttg ttg gaa aca gat gag gct acc cta gat aca agg aaa Glu Ser Gly Leu Leu Glu Thr Asp Glu Ala Thr Leu Asp Thr Arg Lys 110 632 ata gta gaa gct tgt aaa gcc aaa act gat gct ggc ggt gaa gat gct Ile Val Glu Ala Cys Lys Ala Lys Thr Asp Ala Gly Glu Asp Ala 130 125

att ttg caa acc aga act tat gac ctt tac atc act tat gat aaa tat

Ile Leu Gln	Thr Arg Thr	Tyr Asp Leu	Tyr Ile Thr	-	ys Tyr 50
_	cca cga tta Pro Arg Leu 155				_
	gtt gag cac Val Glu His		_	•	
•	gtg acc att Val Thr Ile	•	_	Pro Pro P	
	gtt cac cca Val His Pro 205				
	gtt gca gaa Val Ala Glu 220			/ Val His M	
	ttc ttg aaa Phe Leu Lys 235	-	Ala Val Ile		
_	aca aga cac Thr Arg His	_		agcataaaat	1015
ctatcctaat	tattggttct ga	atttttaaa ga	attaaccc ata	agatgtga co	attgacca 1075
	tatatacagt to				
aatatgttcc	actaccagec ti	tacttgttt aa	taaaaatc agt	igcaaaaa aa	aaaa 1191

<210> 63 <211> 1008 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 657..923 <221> sig\_peptide <222> 657..896 <223> Von Heijne matrix score 3.5 seg RGLLSACAPWGDG/ST <221> polyA\_signal <222> 957..962

<221> polyA site

<222> 974..1008

<400> 63

60 ntcgnatgtg gcacaaaacc cctctgctgg ctcatgtgtg caactgagac tgtcagagca 120 tggctagctc tggggtccag ctctgctggg tgggggctag agaggaagca gggagtatct gcacacagga tgcctgcgct caggtggttg cagaagtcag tgcccaggcc cccccacaca 180 gtccccaaag gtccggcctc cccagcgcgg ggctcctcgt ttgaggggag gtgacttccc teccageagg etettggaca cagtaagett ecceageeet geetgageag cettteetee 360 ttgccctgtt ccccacctcc cggctccagt ccagggagct cccagggaag tggtcgaccc 420 ctccagtggc tgggccactc tgctagagtc catccgccaa gctgggggca tcggcaaggc caagctgcgc agcatgaagg agcgaaagct ggagaagaag aagcagaagg agcaggagca 480 540 agtgagagcc acgagccaag gtgggcactt gatgtcggat ctcttcaaca agctggtcat gaggegeaag ggeatetetg ggaaagaace tggggetggt gaggggeeeg gaggageett 600 tgcccgcgtg tcagactcca tccctcctct gccgccaccg cagcagccac aggtag atg 659 WO 99/31236

				Met
		•		-80
agg aca agg acg	act ggg aat o	cct agg ggg	ctc cat gac acc	ttc ccc 707
Arg Thr Arg Thr	Thr Gly Asn I	-70	Leu His Asp Thr	-65
cgc aga ccc aga	ctt ggc cgt 1	tgc tct gac	atg gac aca gcc	agg aca 755
Arg Arg Pro Arg -60	Leu Gly Arg (	Cys Ser Asp -55	Met Asp Thr Ala -50	Arg Thr
agc tgc tca gac	ctg ctt ccc	tgg gag ggg	gtg acg gaa cca	gca ctg 803
-45		-40	Val Thr Glu Pro	
tgt gga gac cag	ctt caa gga	acg gaa ggc	tgg ctt gag gcc	aca cag 851
Cys Gly Asp Gln	Leu Gin Giy	Thr Glu Gly	Trp Leu Glu Ala -20	ini Gin
cta aga caa aga	ctt ctg tct	gcc tgt gct	cca tgg ggg gac	ggc tcc 899
Leu Gly Arg Gly	Leu Leu Ser	Ala Cys Ala	Pro Trp Gly Asp	Gly Ser
-15	-10	tot taagagg	-5 ctt ccagagaaaa c	1 ggcacacca 953
Thr Gln Pro Val			cee coagagaaaa o	•
_	gagcag aaaaaa	aaaa aaaaaa	aaaa aaaaaaaaa	aaaan 1008
<b></b>				
<210> 64				
<211> 568				
<212> DNA <213> Homo sapi	ens			
<5513> HOMO Bapi	CIIO			•
<220>				
<221> CDS <222> 18311				
<221> sig_pepti	.de			
<222> 1862 <223> Von Heijn	ne matrix			
score 8.4	<u>l</u>			
seq AMWLI	LCVALAVLA/WG			•
<400> 64				
agtgctgctt acco	Met Glu 1	gca atg tgg Ala Met Trp	ctc ctg tgt gtg Leu Leu Cys Val -10	gcg ttg 50 Ala Leu
ara atc tta aca	-15 a too ooc ttc	ctc tag ati	tgg gac tcc tca	<del>-</del>
Ala Val Leu Ala	a Trp Gly Phe	Leu Trp Va.	Trp Asp Ser Ser	Glu Arg
atg aag agt cg	g gag cag gga	gga cgg ct	g gga gcc gaa ag	cgg acc 146
Met Lys Ser Arg	g Glu Gln Gly	Gly Arg Let	ı Gly Ala Glu Se	r Arg Thr
15	a aca cac cct	20 gac gat ga	25 a gcc atg ttt tt	t gct ccc 194
Leu Leu Val Ile	e Ala His Pro	Asp Asp Gl	u Ala Met Phe Ph	e Ala Pro
30	35		40	
aca gtg cta gg	c ttg gcc cgc	cta agg ca	c tgg gtg tac ct	g ctt tgc 242
Thr Val Leu Gly	y Leu Ala Arg 50	Leu Arg H1	s Trp Val Tyr Le 55	d Led Cys
ttc tct qca gt	t ttc cgt agg	gag cta ag	t gaa tac acc ga	a ggt ctt 290
Phe Ser Ala Va	l Phe Arg Arg 65	Glu Leu Se 70	r Glu Tyr Thr Gl	u Gly Leu 75
acc tot daa co			ageggeegge ttae	
Thr Ser Glu Pr			<del></del>	
80				agagaaacag 401
ggttggggga cgt	cggcagc tcgcg	racta cgcca	gcagg attgaggagc	. ayayadacay 401

ttgcagttgg ttgtattcag tacctgcatt tccgttggga actccacctg tacttgttat

461

521 568 ..

totgtggaac ttttttatt tgtagaagga gcaagaatat tgaccttact atatagcaca cgaaacaatc tatgctgtat cgtgcctgct caatccttaa agttaac	521 568
<210> 65	
<211> 538	
<212> DNA <213> Homo sapiens	
22137 NOMO BADIENS	
<220>	
<221> CDS	
<222> 151426	
<221> sig_peptide	•
<222> 151258	
<223> Von Heijne matrix	•
score 5.2 seq KVALAGLLGFGLG/KV	
beg with the second second	
<221> polyA_signal	
<222> 505510	
<221> polyA_site	
<222> 527538	
<400> 65	
	60
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat	60 120
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgcctttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc	
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccacaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val	120
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccacaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35 -30	120
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgcctttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35  -30  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa	120 174
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgcctttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa  Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys  -25  -20  -15	120 174 222
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgcctttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa  Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys  -25  -20  -15  gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac	120 174
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgcctttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa  Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys  -25  -20  -15  gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac  Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr	120 174 222
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgcctttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa  Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys  -25  -20  -15  gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac  Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr  -10  -5	120 174 222
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa  Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys  -25  -20  -15  gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac  Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr  -10  -5  ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt  Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg	120 174 222 270
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa  Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys  -25  -20  -15  gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac  Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr  -10  -5  ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt  Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg  5  10  15  20	120 174 222 270 318
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa  Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys  -25  -20  -15  gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac  Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr  -10  -5  ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt  Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg  5  10  15  20  ggg gct ggt ttt ggt cca cag cat aac agg cac tgc ctc ctt acc tgt	120 174 222 270
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa  Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys  -25  -20  -15  gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac  Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr  -10  -5  ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt  Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg  5  10  15  20	120 174 222 270 318
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc  Met Leu Val Thr Gln Gly Leu Val  -35  -30  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa  Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys  -25  -20  -15  gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac  Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr  -10  -5  ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt  Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg  5  10  15  20  ggg gct ggt ttt ggt cca cag cat aac agg cac tgc ctc ctt acc tgt  Gly Ala Gly Phe Gly Pro Gln His Asn Arg His Cys Leu Leu Thr Cys  25  30  35  gag gaa tgc aaa ata aag cat gga tta agt gag aag gga gac tct cag	120 174 222 270 318
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc Met Leu Val Thr Gln Gly Leu Val -35 -30  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys -25 -20 -15  gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr -10 -5 1  ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg 5 10 15 20  ggg gct ggt ttt ggt cca cag cat aac agg cac tgc ctc ctt acc tgt Gly Ala Gly Phe Gly Pro Gln His Asn Arg His Cys Leu Leu Thr Cys 25 30 35  gag gaa tgc aaa ata aag cat gga tta agt gag aag gga gac tct cag Glu Glu Cys Lys Ile Lys His Gly Leu Ser Glu Lys Gly Asp Ser Gln	120 174 222 270 318
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc Met Leu Val Thr Gln Gly Leu Val -35 -30   tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa  Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys -25 -20 -15   gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac  Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr -10 -5 1   ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt  Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg  5 10 15 20   ggg gct ggt ttt ggt cca cag cat aac agg cac tgc ctc ctt acc tgt  Gly Ala Gly Phe Gly Pro Gln His Asn Arg His Cys Leu Leu Thr Cys  25 30 35   gag gaa tgc aaa ata aag cat gga tta agt gag aag gga gac tct cag  Glu Glu Cys Lys Ile Lys His Gly Leu Ser Glu Lys Gly Asp Ser Gln  40 45 50	120 174 222 270 318
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc Met Leu Val Thr Gln Gly Leu Val -35 -30  tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys -25 -20 -15  gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr -10 -5 1  ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg 5 10 15 20  ggg gct ggt ttt ggt cca cag cat aac agg cac tgc ctc ctt acc tgt Gly Ala Gly Phe Gly Pro Gln His Asn Arg His Cys Leu Leu Thr Cys 25 30 35  gag gaa tgc aaa ata aag cat gga tta agt gag aag gga gac tct cag Glu Glu Cys Lys Ile Lys His Gly Leu Ser Glu Lys Gly Asp Ser Gln	120 174 222 270 318 366 414
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgccttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc Met Leu Val Thr Gln Gly Leu Val -35 -30 tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys -25 -20 -15 gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr -10 -5 1 ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg 5 10 15 20 ggg gct ggt ttt ggt cca cag cat aac agg cac tgc ctc ctt acc tgt Gly Ala Gly Phe Gly Pro Gln His Asn Arg His Cys Leu Leu Thr Cys 25 30 35 gag gaa tgc aaa ata aag cat gga tta agt gag aag gga gac tct cag Glu Glu Cys Ile Lys His Gly Leu Ser Glu Lys Gly Asp Ser Gln 40 45 50 cct tca gct tcc taaattctgt gtctgtgact ttcgaagttt tttaaacctc Pro Ser Ala Ser	120 174 222 270 318 366 414 466
cactgggtca aggagtaagc agaggataaa caactggaag gagagcaagc acaaagtcat catggcttca gcgtctgctc gtggaaacca agataaagat gcccattttc caccaccaag caagcagctc tgcctttttc tcttgtaagc atg ctt gtc acc cag gga cta gtc Met Leu Val Thr Gln Gly Leu Val -35 -30 tac caa ggt tat ttg gca gct aat tct aga ttt gga tca ttg ccc aaa Tyr Gln Gly Tyr Leu Ala Ala Asn Ser Arg Phe Gly Ser Leu Pro Lys -25 -20 -15 gtt gca ctt gct ggt ctc ttg gga ttt ggc ctt gga aag gta tca tac Val Ala Leu Ala Gly Leu Leu Gly Phe Gly Leu Gly Lys Val Ser Tyr -10 -5 l ata gga gta tgc cag agt aaa ttc cat ttt ttt gaa gat cag ctc cgt Ile Gly Val Cys Gln Ser Lys Phe His Phe Phe Glu Asp Gln Leu Arg 5 10 15 20 ggg gct ggt ttt ggt cca cag cat aac agg cac tgc ctc tta acc tgt Gly Ala Gly Phe Gly Pro Gln His Asn Arg His Cys Leu Leu Thr Cys 25 30 35 gag gaa tgc aaa ata aag cat gga tta agt gag aag gga gac tct cag Glu Glu Cys Lys Ile Lys His Gly Leu Ser Glu Lys Gly Asp Ser Gln 40 45 50 cct tca gct tcc taaattctgt gtctgtgact ttcgaagttt tttaaacctc Pro Ser Ala Ser	120 174 222 270 318 366 414

<210> 66

<211> 1747

<212> DNA

<213> Homo sapiens

<221> CDS <222> 10..1062 <221> sig\_peptide <222> 10..57 <223> Von Heijne matrix score 4.9 seq FIYLQAHFTLCSG/WS <221> polyA\_signal <222> 1710..1715 <221> polyA\_site <222> 1735..1747 <400> 66 geeteacea atg gtt ece tte ate tat etg caa gee cae ttt aca ete tgt Met Val Pro Phe Ile Tyr Leu Gln Ala His Phe Thr Leu Cys -10 99 tet ggg tgg tcc agc aca tac cgg gac ctc cgg aag ggt gtg tat gtg Ser Gly Trp Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val 147 ccc tac acc cag ggc aag tgg gaa ggg gag ctg ggc acc gac ctg gta Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val 25 20 age ate ecc cat gge ecc aac gte act gtg egt gee aac att get gee 195 Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala 40 35 atc act gaa tca gac aag ttc ttc atc aac ggc tcc aac tgg gaa ggc 243 Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly 50 291 atc ctg ggg ctg gcc tat gct gag att gcc agg cct gac gac tcc ccg Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Pro 339 gag cct ttc ttt gac tct ctg gta aag cag acc cac gtt ccc aac ctc Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu ttc tcc ctg cag ctt tgt ggt gct ggc ttc ccc ctc aac cag tct gaa 387 Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu 100 105 gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc gac cac 435 Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His 120 115 483 teg etg tac aca gge agt etc tgg tat aca ecc atc egg egg gag tgg Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp 135 130 531 tat tat gag gtg atc att gtg cgg gtg gag atc aat gga cag gat ctg Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu 155 150 579 aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg gac agt Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser 165 627 ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct gca gtc Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val 180 185 175 aaa too ato aag goa goo too too acg gag aag tto cot gac ggt tto 675 Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe 200 205 195 tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc cct tgg 723 Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp

215

771

aac att ttc cca gtc atc tca ctc tac cta atg ggt gag gtt acc aac

210

WO 99/31236

_	-1.	<b>5</b> 1.	1.Jr.	**- 3	T1.	C-~	T 011	Tare	Len	Met	Gly	Glu	٧al	Thr	Asn	
Asn	11e	225	Pro	vaı	116	Sei	230	IYI	Бец	Me C	Gry	Glu 235	141			
cag	tec		cac	atc	acc	atc		ccg	cag	caa	tac	ctg	cgg	cca	gtg	819
Gln	Ser	Phe	Ara	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	
	240					245					250					
gaa	gat	gtg	gcc	acg	tcc	caa	gac	gac	tgt	tac	aag	ttt	gcc	atc	tca	867
Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	
255					260					265					270	03.5
cag	tca	tcc	acg	ggc	act	gtt	atg	gga	gct	gtt	atc	atg	gag	ggc	ttc	915
Gln	Ser	Ser	Thr		Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu	GIA	Pne	
				275				.*	28,0					285	200	963
tac	gtt	gtc	ttt	gat	cgg	gcc	cga	aaa	cga	att	ggc	ממת	212	yet val	agc Ser	. 505
Tyr	Val	Val		qaA	Arg	Ala	Arg	ப்த 295		TTE	GIY	PILE	300	401	Ser	
			290		 	~~~	++0			aca.	aca	ata			ccn	1011
get	Cyc	Vic	yey val	Ui e	yat Asn	Glu	Phe	Ara	Thr	Ala	Ala	Val	Glu	Gly	Pro	•
WIG	Сув	305	V 0.1	1110	vob	014	310			••••		315		•	.*	
ttt	tat		ctt	oga	cat	gga			tgg	cta	caa	cat	tcc	aca	gac	1059
Phe	Cvs	His	Leu	Gly	His	Gly	Arg	Leu	Trp	Leu	Gln	His	Ser	Thr	Asp	
	320				.*	325		• •	· · · · ·	•'	330	ı				
aga	tga	gtca	acc	ctca	tigac	ca t	agcc	tatg	t ca	tggc	tgcc	atc	tgcg	CCC		1112
Arg		_								•	•					
335																
tct	tcat	gct	gcca	ctct	gc c	tcat	ggtg	t gt	cagt	ggcg	cto	cctc	cgc	tgcc	tgcgcc	1172 1232
ago	agca	tga	tgac	tttg	ct g	atga	cato	tcc	ctgo	tgaa	gte	agga	ggc	ccat	gggcag	1232
aag	atag	gga	ttcc	cctg	ga c	caca	CCTC	c gt	ggtt	Cact		gtca	Caa	tace	gagaca	1352
cag	atgg	Cac	ctgt	ggcc	ag a	gcac	CLCa	ig ge	1000L	2000	act	.cacc	cta	tage	tctgcc	1412
ttg	atgg	aga	agga	2222	ge t	ctoo	tagge	9 95	aata	ctct	tac	tcac	ctc	aaat	agacag ttaagt	1472
aaa	agag	ttc	toct	aayu	מם ב	actt	cago	e et	gaac	cttt	ato	acca	ttc	cttt	aaattc	1532
to	Saca	caa	agta	ttct	tc t	tttc	ttac	t tt	cage	aqta	cto	gcat	cac	acgo	caggtta	1592
cct	taac	ata	tate	ccto	ita c	taco	ctac	c ac	gagaa	igaga	a cca	agct	tgt	ttc	ctgctg	1652
qc	aaac	tca	gtac	gaga	igg a	tgca	cagt	t to	ctat	ttg	, tti	agag	jaca	ggga	actgtat	1712
			aaca													1747

<210> 67 <211> 1686 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 78..491 <221> sig\_peptide <222> 78..218 <223> Von Heijne matrix score 5.8 seq LMCFGALIGLCAC/IC <221> polyA\_signal <222> 1652..1657 <221> polyA\_site <222> 1673..1686

```
-45
                                                                      158
age ggg att gat etc ett agg ace tat ett tgg egt tge eag tte ett
Ser Gly Ile Asp Leu Leu Arg Thr Tyr Leu Trp Arg Cys Gln Phe Leu
                                            -25
                        -30
    -35
                                                                      206
tta cct ttt gtg agt tta ggt ttg atg tgc ttt ggg gct ttg atc gga
Leu Pro Phe Val Ser Leu Gly Leu Met Cys Phe Gly Ala Leu Ile Gly
                                         -10
                     -15
-20
ctt tgt gct tgc att tgc cga agc tta tat ccc acc att gcc acg ggc
Leu Cys Ala Cys Ile Cys Arg Ser Leu Tyr Pro Thr Ile Ala Thr Gly
                1
att ctc cat ctc ctt gca ggt ctg tgt aca ctg ggc tca gta agt tgt
                                                                      302
Ile Leu His Leu Leu Ala Gly Leu Cys Thr Leu Gly Ser Val Ser Cys
                            20
        15
tat gtt gct gga att gaa cta ctc cac cag aaa cta gag ctc cct gac
Tyr Val Ala Gly Ile Glu Leu Leu His Gln Lys Leu Glu Leu Pro Asp
                                                                      398
aat gta tcc ggt gaa ttt gga tgg tcc ttc tgc ctt gct tgt gtc tct
Asn Val Ser Gly Glu Phe Gly Trp Ser Phe Cys Leu Ala Cys Val Ser
                                         55
                     50
get ecc tta cag tte atg get tet get etc tte ate tgg get get cae
                                                                       446
Ala Pro Leu Gln Phe Met Ala Ser Ala Leu Phe Ile Trp Ala Ala His
                                     70
                                                                      491
acc aac cgg aga gag tac acc tta atg aag gca tat cgt gtg gca
Thr Asn Arg Arg Glu Tyr Thr Leu Met Lys Ala Tyr Arg Val Ala
                                 85
 tgagcaagaa actgcctgct ttacaattgc catttttatt tttttaaaat aatactgata
                                                                       551
 ttttccccac ctctcaattg tttttaattt ttatttgtgg atataccatt ttattatgaa
                                                                       611
 aatctatttt atttatacac attcaccact aaatacacac ttaataccac taaaatttat
                                                                       671
 gtggtttact ttaagcgatg ccatctttca aataaactaa tctaggtcta gacagaaaga
                                                                       731
 aatggataga gacttgacac aaatttatga aagaaaattg ggagtaggaa tgtgaccgaa
                                                                       791
 aacaagttgt gctaatgtct gttagacttt tcagtaaaac caaagtaact gtatctgttc
                                                                       851
 aactaaaaac totatattag tttotttggg aaacctotca togtcaaaac tttatgttca
                                                                       911
 ctttgctgtt gtagatagcc agtcaaccag cagtattagt gctgttttca aagatttaag
                                                                       971
 ctctataaaa ttgggaaatt atctaagatc attttcccta agcattgaca catagcttca
 tctgaggtga gatatggcag ctgtttgtat ctgcactgtg tctgtctaca aagagtgaaa
 aatacagtgt ttacttgaaa ttttaacttt gtaactgcaa gaattccagt tcggccgggc
 gaggattagt attattttta actctccgta agattttcag taccaccaaa ttgttttgga
                                                                      1211
 tttttttttt ttcctcttca cataccaggg ttattaaaag tgtgctttct ttttacatta
                                                                      1271
 tattacagtt acaaggtaaa attcctcaac tgctatttat ttattccagc ccagtactat
 aaagaacgtt tcaccataat gaccctccag agctgggaaa cctaccacaa gatctaaagt
                                                                      1391
 tetggetgte cattaacete caactatggt etttattet tgtggtaata tgatgtgeet
                                                                      1451
 ttccttgcct aaatcccttc ctggtgtgta tcaacattat ttaatgtctt ctaattcagt
                                                                      1511
 cattttttat aagtatgtct ataaacattg aactttaaaa aacttattta tttattccac
                                                                      1571
 tactgtagca attgacagat taaaaaaatg taacttcata atttcttacc ataacctcaa
                                                                      1631
                                                                      1686
 tgtcttttt aaaaaataaa attaaaaatg aaaagagacc caaaaaaaaa aaaaa
```

```
<210> 68
<211> 542
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 69..371

<221> sig_peptide
<222> 69..287
<223> Von Heijne matrix
score 4
```

seq AVGFLFWVIVLTS/WI

<221> polyA_signal <222> 510515	•••
<221> polyA_site <222> 530542	
<400> 68	a 60
tgttacttag ggtcaaggct tgggtcttgc cccgcaaacc cttgggacga cccggccccagcgcagct atg aac ctg gag cga gtg tcc aat gag gag aaa ttg aac ctg	110
Met Asn Leu Glu Arg Val Ser Asn Glu Glu Lys Leu Asn Leu -70 -65 -60	
tgc cgg aag tac tac ctg ggg ggg ttt gct ttc ttg cct ttt ctc tgg  Cys Arg Lys Tyr Tyr Leu Gly Gly Phe Ala Phe Leu Pro Phe Leu Trp  -55  -50  -45	158
ttg gtc aac atc ttc tgg ttc tac cga gag gcc ttc ctt gtc cca gcc Leu Val Asn Ile Phe Trp Phe Tyr Arg Glu Ala Phe Leu Val Pro Ala -40 -35 -30	206
tac aca gaa cag agc caa atc aaa ggc tat gtc tgg cgc tca gct gtg Tyr Thr Glu Gln Ser Gln Ile Lys Gly Tyr Val Trp Arg Ser Ala Val -25 -20 -15	254
ggc ttc ctc ttc tgg gtg ata gtg ctc acc tcc tgg atc acc atc ttc Gly Phe Leu Phe Trp Val Ile Val Leu Thr Ser Trp Ile Thr Ile Phe -10 -5 1 5	302
cag atc tac cgg ccc cgc tgg ggt gcc ctt ggg gac tac ctc tcc ttc Gln Ile Tyr Arg Pro Arg Trp Gly Ala Leu Gly Asp Tyr Leu Ser Phe 10 15 20	350
acc ata ccc ctg ggc acc ccc tgacaacttc tgcacatact ggggccctgc Thr Ile Pro Leu Gly Thr Pro 25	401
ttattctccc aggacaggct ccttaaagca gaggagcctg tcctgggagc cccttctca	a 461
actectaaga ettetteta tetecaeet teteteetga catececcaa taaaggace	c 521
taactttcaa aaaaaaaaa a	542
<210> 69 <211> 1174 <212> DNA <213> Homo sapiens	
<220>	
<221> CDS	
<222> 2757	
<221> sig_peptide <222> 2205 <223> Von Heijne matrix     score 7.3     seq LRLILSPLPGAQP/QQ	
<221> polyA_site <222> 11601174	
<pre>&lt;400&gt; 69 g atg cct gag ggc ccc gag ctg cac ctg gcc agc cag ttt gtg aat g Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn G</pre>	ag 49 lu
-65 -60 -55 gcc tgc agg gcg ctg gtg ttc ggc ggc tgc gtg gag aag tcc tct gtc Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val	97
-50 -45 -40 ago ogo aac oot gag gtg ooc ttt gag ago agt goo tac ogo ato toa	145

Ser		Asn	Pro	Glu	Val	Pro	Phe	Glu	Ser	Ser	Ala -25	Tyr	Arg	Ile	Ser	
4-	-35	gcc			220		cta	cac	cta	ata		agc	cct	ctq	cct	193
gct	tca	gcc Ala	cgc	ggc	Tue	Clu	Leu	Ara	Len	Tle	Leu	Ser	Pro	Leu	Pro	
	ser	Ala	Arg	GIY		Glu	Den	AT 9	БСС	-10	200				-5	
-20					-15				~~~		atc	ttc	cac	ttc	_	241
999	gcc	cag	cct	caa	cag	gag	cca	teg	31-	Tan	37.1	Dhe	yra	Dhe	Glv	
Gly	Ala	Gln	Pro	Gin	Gin	GIU	PIO	Ten	Ala	Leu	vaı	PIIC	10	1	Cly	
				1				<b>5</b>			~~~	ata		cac	cat	289
atg	tcc	ggc	tct	ttt	cag	ctg	gtg	ccc	cgc	gag	gag	Tan	Dra	720	Uie	203
Met	Ser	Gly	Ser	Phe	Gln	Leu		Pro	Arg	GIU	GIU	neu	PIO	Arg	ure	
		15					20	•				25		~~~	<b>a</b> t a	337
gcc	cac	ctg	cgc	ttt	tac	acg	gcc	ccg	cct	ggc	CCC	cgg	CLC	315	Tou	557
Ala	His	Leu	Arg	Phe	Tyr		Ala	Pro	Pro	GIÀ	Pro	Arg	ьeu	Ala	Ten .	
	30					35		٠			40					205
tgt	ttc	gtg	gac	atc	cgc	cgg	ttc	ggc	cgc	tgg	gac	ctt	999	gga	aag	385
Cys	Phe	Val	Asp	Ile	Arg	Arg	Phe	Gly	Arg	Trp	Asp	Leu	GIA	GIY	гув	
45					50					55					60	
taa	cag	ccg	ggc	cgc	999	CCC	tgt	gtc	ttg	cag	gag	tac	cag	cag	ttc	433
Tro	Gln	Pro	Gly	Arg	Gly	Pro	Cys	Val	Leu	Gln	Glu	Tyr	Gln	GID	Phe	•
				65					70					75		
agg	gag	aat	ata	cta	cga	aac	cta	gcg	gat	aag	gcc	ttt	gac	cgg	CCC	481
Ara	Glu	Asn	Val	Leu	Arq	Asn	Leu	Ala	Asp	Lys	Ala	Phe	Asp	Arg	Pro	•
••• =	0_0		80		_			85	_	-		,	90			
atc	tac	gag	acc	ctc	cta	qac	caq	agg	ttc	ttc	aat	ggc	att	ggc	aac	529
Tle	Cvs	Glu	Ala	Leu	Leu	Asp	Gln	Arg	Phe	Phe	Asn	Gly	Ile	Gly	Asn	
110	Cys	95					100					105				
+-+	cto	COO	aca	gag	atc	cta			ctq	aaq	ato	ccc	ccc	ttt	gag	577
Tire	Leu	720	Δla	Glu	Tle	Leu	Tvr	Ara	Leu	Lys	Ile	Pro	Pro	Phe	Glu	
TYL	110		7124	-		115				•	120	)				•
	110		tea	atc	cta			cta	cac	cac	cac	aqo	CCC	ago	ccg	625
aag	21-	2~~	Sex	. Wal	1.011	ເງນ	Δla	Leu	Gln	Glr	His	Arc	Pro	Ser	Pro	
-		Arg	Jei		130					135	;	_	,		140	
125			~+ <i>~</i>		220		ata	200	acc			cac	aat	tca	gac	673
gag	CEG	acc	Tou	age	Cas	Larg	716	Arc	Thr	Tave	ilei	Glr	Asr	sei	Asp	
GIU	Let	ini	Leu	145		шур	110	S	150	. <u>-</u>				155	5	
						. +c=	ato				ate	a ata	cac	tto	ggt	721
Ctg	CCC	gag	CLA	cgt	. cac		. 3723	Dro	Lare	, ga	· ye:	l Vai	Gla	Lei	Gly	
Leu	ı Let	ı GIU			nıs	) DET	. va.	165		, 61	, vu.		170	)	3	
			160									e ta:				767
gag	ggc	aaa	gat	ggc	ago	: aac		· cyc	. Db.	. ago	. aa	a cy	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	-9		
Glu	ı Ala	Lys		GT?	Sei	ASI			PIR	: DE.	Luy	5				
		175	j				180						+	+ ~+	acceta	827
acc	cctg	gggc	actt	gtco	cc c	ctctg	ggac	et ga	ICCC	accg	a LL	Lyya	agee	cto	agcccta	887
gct	tgata	actc	aato	ggact	ag g	gccto	CCEC	ac ti	gtc	aata	gtg		cagg	200	ggcgcag	947
tg	gctc	atgc	ctgt	ggt	cc s	gcad	cttc	39 9°	aggc	cgag	- gg	9959	gete	acc	tgaggtc	1007
agg	gagt	tcga	gaco	catco	tg 9	gccaa	acat	gg t	gaaa	CCC	a tc	tcca	ctaa	aat	gcaaaaa	1067
ati	tage	cago	tata	atac	icq (	gcad	cctg	ta gi	tctc	agct.	a ct	cggg	agga	tga	ggcagga	1127
aaa	atco	ctta	aaco	ccaq	ag d	gtgga	aggt:	tg ca	agtt	gagc	t ga	gatc	gtgc	cat	tgcactc	
ca	gcct	gggc	aac	gagag	gca a	aaact	tcca	tc to	caaa	aaaa	a aa	aaaa	a			1174

<210> 70

<211> 1285

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 2..1051

<221> sig\_peptide

<222> 2..205

WO 99/31236 -48- PCT/IB98/02122 -

<223> Von Heijne matrix score 7.3 seg LRLILSPLPGAQP/QQ <221> polyA\_signal <222> 1248..1253 <221> polyA\_site <222> 1272..1285 <400> 70 g atg cct gag ggc ccc gag ctg cac ctg gcc agc cag ttt gtg aat gag . Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu 97 gcc tgc agg gcg ctg gtg ttc ggc ggc tgc gtg gag aag tcc tct gtc Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val -45 age ege aac cet gag gtg eee ttt gag age agt gee tae ege ate tea 145 Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser -25 -30 get tea gee ege gge aag gag etg ege etg ata etg age eet etg eet . 193 Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro -15 -10 ggg gcc cag ccc caa cag gag cca ctg gcc ctg gtc ttc cgc ttc ggc 241 Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly atg tcc ggc tct ttt cag ctg gtg ccc cgc gag gag ctg cca cgc cat 289 Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His 337 gcc cac ctg cgc ttt tac acg gcc ccg cct ggc ccc cgg ctc gcc cta Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu tgt ttc gtg gac atc cgc cgg ttc ggc cgc tgg gac ctt ggg gga aag 385 Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys 55 50 45 tgg cag ccg ggc cgc ggg ccc tgt gtc ttg cag gag tac cag cag ttc 433 Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Gln Glu Tyr Gln Gln Phe 70 agg ctg aag atc ccc ccc ttt gag aag gcc cgc tcg gtc ctg gag gcc 481 Arg Leu Lys Ile Pro Pro Phe Glu Lys Ala Arg Ser Val Leu Glu Ala ctg cag cac agg ccg agc ccg gag ctg acc ctg agc cag aag ata 529 Leu Gln Gln His Arg Pro Ser Pro Glu Leu Thr Leu Ser Gln Lys Ile 100 577 agg acc aag ctg cag aat cca gac ctg ctg gag cta tgt cac tca gtg Arg Thr Lys Leu Gln Asn Pro Asp Leu Leu Glu Leu Cys His Ser Val 120 115 ccc aag gaa gtg gac cag ttg ggg ggc agg ggc tac ggg tca gag agc 625 Pro Lys Glu Val Asp Gln Leu Gly Gly Arg Gly Tyr Gly Ser Glu Ser 130 ggg gag gag gac ttt gct gcc ttt cga gcc tgg ctg cgc tgc tat ggc 673 Gly Glu Glu Asp Phe Ala Ala Phe Arg Ala Trp Leu Arg Cys Tyr Gly 150 721 atg cca ggc atg agc tcc ctg cag gac cgg cat ggc cgt acc atc tgg Met Pro Gly Met Ser Ser Leu Gln Asp Arg His Gly Arg Thr Ile Trp 165 160 769 ttc cag ggg gat cct gga ccg ttg gca ccc aaa ggg cgc aag tcc cgc Phe Gln Gly Asp Pro Gly Pro Leu Ala Pro Lys Gly Arg Lys Ser Arg 180 817 aaa aag aaa tcc aag gcc aca cag ctg agt cct gag gac aga gtg gag Lys Lys Lys Ser Lys Ala Thr Gln Leu Ser Pro Glu Asp Arg Val Glu

200

WO 99/31236 PCT/IB98/02122 -

gac Asp	gct Ala	ttg Leu	cct, Pro	Pro	Ser	aag Lys	gcc Ala	cct Pro	tcc Ser	ГÀг	aca Thr	cga Arg	agg Arg	gc Al	a n	ag ys 20	865
205					210					215					_		012
aqa	qac	ctt	cct	aag	agg	act	gca	acc	cag	cgg	cct	gag	999	ac	c a	gc	913
Ara	Asp	Leu	Pro	Lys	Arg	Thr	Ala	Thr	Gln	Arg	Pro	Glu	Gly	Th	r S	er	
				225					230					23	2		
			gac	cca	caa	act	ccc	aca	ata	ccc	aaq	aag	ggg	ag	g a	gg	961
7	Cay	Cag	Asp	Dro	Glu	Ala	Pro	Thr	Val	Pro	Lvs	Lvs	Gly	Ar	g A	rg	
Leu	GID	GIII		PIO	GIU	AIG	110	245			-1-	-,-	250		_	_	
			240						+	242	000				c a	ag	1009
aag	999	cga	cag	gca	gcc	CCT	ggc	Cac	Cuc	aya	7000	722	Tuc	Va	ו ד	vs vs	
Lys	Gly	Arg	Gln	Ala	Ala	Ser	GIĀ	His	Cys	Arg	PIO	Arg	пλр	٧a	יי די	ys	
		255		•			260		•			265					3053
act	qac	atc	cca	tcc	ttg	gaa	cca	gag	999	acc	tca	gcc	tct				1051
Δla	Asp	Ile	Pro	Ser	Leu	Glu	Pro	Glu	Gly	Thr	Ser	Ala	Ser	•			
7.10	270					275					280						
· -	270		ctctc	cttc	c ti		tca	c cc	tttc	ttat	tat	cttq	ccc	tgo	cato	tggg	1111
tag	cayy	agg '			,	7622	etc	t da	aggt	gcaa	aca	aacc	ctá	cac	acto	ttcc	1171
ggt	ctga	att	tttgg	gage	a g	gCaat	acc	c ga	2990			2500	222	act	cet	ataa	1231
ctg	caca	act	ctcat	ggtt	it ta	aatt	gtac	CCC	atet	teca	Cat		aaa	900		gtga	1285
aaa	atgc	tgc .	attt	taat	ta a	actga	atac	a tt	tgaa	ctcc	aaa	aaaa	aaa	aaa	aa		1265
	_	_															
				•					•	•							
		_										٠					
	0> 7													•			
<21	1> 1	398															
<21	2> D	NA															
<21	3> H	omo	sapie	ens													
	_		-														
-22	0																
<22																	
_	1> 0			. '									•				
<22	2> 2	211	71														
<22	21> 8	sig p	epti	de													
		220															
			eijn	e ma	trix												
<22			7.3		U												
					~ » ~ »	/00											
	2	seq I	RLIL	SPLP	GAQI	'/ QQ											
<22	21> 1	polyA	_sig	nal													
			.137														•
- 2 1	21	7117		_													
			Lsit														
<2	22>	1386	.139	8													
<4	00>	71															
a	atq	cct o	ag g	gc c	cc g	gag c	tg	cac	ctg	gcc a	agc	cag	ttt	gts	g aa	t gag	49
1	Met	Pro (	slu G	Īv F	ro	3lu I	Jeu ∶	His	Leu :	Ala :	Ser	Gln	Phe	Va]	l As	n Glu	
•				65					-60					-55	5		
			g gcg		- ~+,	. ++	- 00	c	c ta	c at	o ga	σ aa	a to	c t	tct	atc	97
gc	c tg	c ag	g geg	י כנק	9 9 5	3 200	99	. 99	~.	- 17-	3 50	, T	- Ce	· ·	Ser	์ Val	
Al	а Су		g Ala	Let	ı va.	r bue			у Су	o va	1 61	ά υγ	ر م	'		,	
		-5	0				-4					- 4	-		_ 4	<b>.</b>	3 4 5
aq	c ca	c aa	c cct	gag	ggt	g cco	: tt	t ga	g ag	c ag	t gc	c ta	C C	gc a	atc	cca	145
Se	r Ar	a As	n Pro	Gli	ı Va	l Pro	o Ph	e Gl	u Se	r Se	r Al	a Ty	r Ai	rg :	lle	Ser	
50	-3	_	<b>-</b> -			-30					-2	5					
	-3	-	c cgo					a .c.	C C+	g =+	_	_	וכ כי	et (	cta	cct	193
gc	t to	a gc	c cgo	: 990	aa	2 24		9 79	,	3 GL	A 7-	2 65	ים בי	ro	יים.ז	Pro	_
		r Al	a Arg	GT)			и ре	u AI	а те	u 11	c he	u ot			يا ټايم	-5	
- 2	0				-1					- 1						_	247
qc				· car	a ca	g ga	g cc	a ct	g go	c ct	g gt	c tt	c c	gc	ttc	ggc	241
~~	g go	c ca	g ccc						_				_				
(4) ∣	g go	c ca a Gl	g eed n Pro	Gl	n Gl	n Gl	u Pr	o Le	eu Al	a Le	u Va	al Pi	ne A	rg	Phe	Gly	
GI	y Al	c ca la Gl	n Pro	Gl	n Gl	n Gl	u Pr	:0 Le 5	u Al	a Le	u Va	al Pi	ne A: 1	rg O	Phe	Gly	
	y Al	a Gl	n Pro	Gl:	n Gl	n Gl	u Pr	5		a Le	u Va	al Pi	ne A:	0	Pne	GIY	289
at	y Al	la Gl	n Pro	Gli 1 t tt	n Gl t ca	n Gl	u Pr a at	5 :g cc	:c c	a Le	u Va ig ga	al Pi	ne Ai 1 tg C	0 ca	cgc	cat	289

WO 99/31236 -50- PCT/IB98/02122 .

gcc cac															337
Ala His 30	Leu	Arg	Phe	Tyr	Thr 35	Ala	Pro	Pro	Gly	Pro 40	Arg	Leu	Ala	Leu	
tgt ttc	gtg	gac	atc	cgc	cgg	ttc	ggc	cgc	tgg	gac	ctt	999	gga	aag	385
Cys Phe	Val	Asp	Ile	Arg	Arg	Phe	Gly	Arg	Trp	Asp	Leu	Gly	Gly	Lys	
45				50	٠.				55	_		_	-	60	
tgg cag	ccg	ggc	cgc	999	ccc	tgt	gtc	ttg	cag	gag	tac	cag	cag	ttc	433
Trp Gln															
_			65	_		•		70	•		•		75		
agg gag	aat	gtg	cta	cga	aac	cta	qcq	gat	aaq	qcc	ttt	qac	caa	ccc	481
Arg Glu															
•		80	10	•			85	•				90			
atc tgc	gag	gcc	ctc	ctq	gac	caq	agg	tic	ttc	aat	aac	att	aac	aac ·	529
Ile Cys	Glu	Ala	Leu	Leu	Asp	Gln	Arg	Phe	Phe	Asn	Glv	Ile	Glv	Asn	
•	95			٠.,	•	100	., -				105		2	••	
tat ctg	cgg	gca	gag	atc	ctq	tac	caa	cta	aaq	atc	CCC	ccc	ttt	gag	577
Tyr Leu															
110	-				115	•	_		•	120					
aag gcc	cqc	tcg	qtc	ctq	qaq	acc	cta	caq	cag	cac	agg	cca	agc	cca	625
Lys Ala															
125	•		"	130					135		5			140	
gag ctg	acc	ctq	agc	•	aag	ata	agg	acc		cta	caq	aat	cca		673
Glu Leu	Thr	Leu	Ser	Gln	Lvs	Ile	Ara	Thr	Lvs	Leu	Gln	Asn	"Pro	Asp	0.0
			145		-7-		5	150	-,-		· · · ·		155		
ctg ctg	qaq	cta	tat	cac	tca	ata	ccc		gaa	ata	atc	caq		aga .	721
Leu Leu	Glu	Leu	Cvs	His	Ser	Val	Pro	Lvs	Glu	Val	Val	Gln	Leu	Glv	
		160	- 2				165	-7-		,		170		7	
ggc aga	aac		aga	tca	gag	aσc		gag	gag	gac	ttt		acc	ttt	769
Gly Arg															
	175	- 2 -	2			180	,				185				
cga gcc		cta.	cac	tac	tat		atd	cca	aac	ato		tcc	cta	cag	817
Arg Ala															<b>.</b>
190	•		3	-2-	195	2			,	200					
gac cgg	cat	qqc	cat	acc		taa	ttc	caq	aaa.		cct	aga	cca	tta	865
Asp Arg															
205		•		210		•			215			2		220	
gca ccc	aaa	999	cgc	aag	tcc	cgc	aaa	aaq	aaa	tcc	aaq	qcc	aça	caq	913
Ala Pro															
	•	•	225	•		•	-	230	•		•		235		
ctg agt	cct	gag	gac	aga	gtg	gag	gac	gct	ttg	cct	ccg	agc	aag	gcc	961
Leu Ser															
		240	-	_			245					250	-		
cct tcc	agg	aca	cga	agg	gca	aag	aga	gac	ctt	cct	aag	agg	act	gca	1009
Pro Ser															
	255					260		_			265	_			
acc cag	cgg	cct	gag	999	acc	agc	ctc	cag	cag	gac	cca	gaa	gct	ccc	1057
Thr Gln	Arg	Pro	Glu	Gly	Thr	Ser	Leu	Gln	Gln	Asp	Pro	Glu	Ala	Pro	
270					275					280					
aca gtg	CCC	aag	aag	999	agg	agg	aag	<b>ggg</b>	cga	cag	gca	gcc	tct	ggc	1105
Thr Val	Pro	Lys	Lys	Gly	Arg	Arg	Lys	Gly	Arg	Gln	Ala	Ala	Ser	Gly	
285				290					295					300	
cac tgc	aga	ccc	cgg	aag	gtc	aag	gct	gac	atc	cca	tcc	ttg	gaa	cca	1153
His Cys	Arg	Pro	Arg	Lys	Val	Lys	Ala	Asp	Ile	Pro	Ser	Leu	Glu	Pro	
			305					310					315		
gag ggg	acc	tca	gcc	tct	tag	cagg	agg	ctct	cctt	gc t	tgca	ctca	С		1201
Glu Gly										_	_				
		320					٠.								
cctttct	tat	tgtc	ttgc	cc te	gcat	ctgg	9 99	tctg	aatt	ttt	ggga	gca	ggca	atatct	1261
gaaggtg															1321
ccatctt															1381
tttgaaa						_			-						1398

WO 99/31236

```
<210> 72
<211> 821
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 42..611
<221> sig_peptide
<222> 42..287
<223> Von Heijne matrix
      score 4.4
      seq NLPHLQVVGLTWG/HI
<221> polyA_signal
<222> 787..792
<221> polyA_site
<222> 808..821
<400> 72
 cegttgccag ttctgcgcgt gtcctgcgtc tccagtatgg a atg tat gtt tgg ccc
                                              Met Tyr Val Trp Pro
 tgt gct gtg gtc ctg gcc cag tac ctt tgg ttt cac aga aga tct ctg
                                                                      104
 Cys Ala Val Val Leu Ala Gln Tyr Leu Trp Phe His Arg Arg Ser Leu
                             -70
         -75
 cca ggc aag gcc atc tta gag att gga gca gga gtg agc ctt cca gga
 Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala Gly Val Ser Leu Pro Gly
                                             -50
                         -55
     -60
 att ttg act gcc aaa tgt ggt gca gaa gta ata ctg tca gac agc tca
                                                                       200
 Ile Leu Thr Ala Lys Cys Gly Ala Glu Val Ile Leu Ser Asp Ser Ser
                                          -35
                     -40
 gaa ctg cct cac tgt ctg gaa gtc tgt cgg caa agc tgc caa atg aat
                                                                       248
 Glu Leu Pro His Cys Leu Glu Val Cys Arg Gln Ser Cys Gln Met Asn
                                      -20
              - 25
 aac ctg cca cat ctg cag gtg gta gga cta aca tgg ggt cat ata tct
                                                                       296
 Asn Leu Pro His Leu Gln Val Val Gly Leu Thr Trp Gly His Ile Ser
                                  -5
 tgg gat ctt ctg gct cta cca cca caa gat att atc ctt gca tct gat
                                                                       344
 Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp Ile Ile Leu Ala Ser Asp
                         10
  gtg ttc ttt gaa cca gaa gat ttt gaa gac att ttg gct aca ata tat
                                                                       392
  Val Phe Phe Glu Pro Glu Asp Phe Glu Asp Ile Leu Ala Thr Ile Tyr
                                          30
                      25
  ttt ttg atg cac aag aat ccc aag gtc caa ttg tgg tct act tat caa
                                                                        440
  Phe Leu Met His Lys Asn Pro Lys Val Gln Leu Trp Ser Thr Tyr Gln
                                      45
                  40
  gtt agg agt gct gac tgg tca ctt gaa gct tta ctc tac aaa tgg gat
                                                                        488
  Val Arg Ser Ala Asp Trp Ser Leu Glu Ala Leu Leu Tyr Lys Trp Asp
                                  60
  atg aaa tgt gtc cac att cct ctt gag tct ttt gat gca gac aaa gaa
                                                                        536
  Met Lys Cys Val His Ile Pro Leu Glu Ser Phe Asp Ala Asp Lys Glu
                              75
  gat ata gca gaa tot acc ott cca gga aga cat aca gtt gaa atg otg
                                                                        584
  Asp Ile Ala Glu Ser Thr Leu Pro Gly Arg His Thr Val Glu Met Leu
                          90
  gtc att tcc ttt gca aag gac agt ctc tgaattatac ctacaacctg
                                                                        631
   Val Ile Ser Phe Ala Lys Asp Ser Leu
```

WO 99/31236 -52 - PCT/IB98/02122

100			برا	:	105												
															cactț gatgt	691 751	
cacc	taga	ca a									_				taaaa	811	
aaaa	aaaa	aa									•					821	
<210	> 73		. •										•				
	> 91 > DN																
	> Ho	_	apie	ns													
<b>ċ220</b>	_		<i>;</i> ·						·							•	
	> CD	S						٠.									
<222	> 62	91	6										٠				
	> si	_	-	e										•			
	> 62			mat:	riv											,	
\		ore	- ,		,~					•							
	se	q LV	TPAA	LRPL	VLG/	GN											
<221	> po	lyA_	site													•	
<222	> 90	49	16														
	> 73																
															gctct g ata	60 109	
		у Су					r Th					g Il			s Ile	100	
												gaa	tat	gtg		157	
Asp	Trp -215	Tnr	Leu	ser :	Pro	Gly -210		His	Ala	_	Asp -205		Tyr	Val	Leu		
tac	tat	tac	tcc	aat	ctc	agt	gtg	cct	att	999	cgc	ttc	cag	aac	cgc	205	
-200		ıyr	ser		ьеи -195		vaı	Pro	11e	-190		Phe	GIn	Asn	Arg -185		
gta	cac									gat	ggc			ctg	ctc	253	
Val	His	Leu	Met	-180	_	Asn	Leu	Cys	Asn -175	_	Gly	Ser	Leu	Leu -170			
									acc	tat				atc	cgc	301	
Gin	Asp	Val	GIN -165		Ala	Asp	Gin	-160		Tyr	Ile	Cys	Glu -15!	Ile	Arg		
								aag	aag				ctg	cat		349	
Leu		Gly -150		Ser	Gln	Val	Phe -145		Lys	Ala	Val	Val -140		His	Val		
ctt	cca	gag	gag	ccc	aaa	gag	ctc	atg	gtc	cat	gtg	ggt	gga	ttg	att	397	
Leu	Pro -135		Glu	Pro	Lys	Glu -130		Met	Val	His	Val -125		Gly	Leu	Ile		
	atg	gga				cag	agc				aaa	cac		acc		445	
Gln -120		Gly	Сув	Val	Phe - 115		Ser	Thr	Glu	Val -11	_	His	Val	Thr	Lys -105		
gta	gaa				tca	gga				aag	gag			gta	ttt	493	
Val	Glu	Trp	Ile	Phe -100		Gly	Arg	Arg	Ala -95	Lys	Glu	Glu	Ile	Val -90	Phe		
cgt	tac	tac	cac			agg	atg	tct		gag	tac	tcc	cag	agc	tgg	541	
														Ser			
ggc	cac	ttc	cag	aat	cgt	gtg	aac	ctg	gtg	ggg	gac	att	ttc	cgc	aat	589	
Gly	His	Phe - 70	Gln	Asn	Arg	Val	Asn	Leu	Val	Gly	Asp	Ile	Phe	Arg	Asn		
gac	ggt		atc	atg	ctt	caa	-65 gga	gtg	agg	gag	tca	-60 gat	gga	gga	aac	. 637	
									_	_							

																	·
Asp G	-55		'*1			-50					-45						
tac a	3.0.0	tqc	agt '	atc	cac	cta	999	aac	ctg	gtg	ttc	aag	aaa	acc	: a	tt	685
Tyr 1	Thr	Cys	Ser	Ile	His	Leu	Gly	Asn	Leu	Val	Phe	Lys	Lys	Thr	. 1	Te	
-40					-35					-30					-	25	722
gtg	ctg	cat	gtc	agc	ccg	gaa	gag	cct	cga	aca	ctg	gtg	acc	CCC	9	ca	733
Val I	Leu	His	Val		Pro	Glu	Glu	Pro	Arg	Thr	Leu	vaı	Thr	-10	) A	14	
				-20					-15			~+~	2+0			ta	781
gcc	ctg	agg	cct	ctg	gtc	ttg	ggt	ggt	aat	cag	Ten	y Ly	מננ פוד	TI	- 9 - V	'al	
Ala	Leu	Arg	-5	Leu	vaı	ьeu	GIÀ	1	ASII	6111	пец	5	110		•		
gga i	-++	a+ c		acc	a.c.a	atc	cta		ctc	cct	atc	ctq	ata	tt	ga	tc	829
gga Gly	ali Tle	val	Cvs	Ala	Thr	Ile	Leu	Leu	Leu	Pro	Val	Leu	Ile	Let	ı I	le	
_	10	Val	<b>C J D</b>			15					20						
ata	220	aaq	acc	tqt	qga	aat	aag	agt	tca	gtg	aat	tct	aca	gt	c t	tg:	877
Val	Lys	Lys	Thr	Cys	Gly	Asn	Lys	Ser	Ser	Val	Asn	Ser	Thr	Va	1 1	eu	
25					30					35			,		4	10	03.6
gtg	aag	aac	acg	aag	aag	act	aat	cca	aaa	aaa	aaa	aaa	1				916
Val	Гуs	Asn	Thr		Lys	Thr	Asn	Pro		Lys	Lys	Lys	5				•
				45					50								
				•	•				•	•							
0.7.0	. 7													•			
<210																	
<211 <212																	
			sapi	ens													
\213		J	F -								•						
<220	)>																•
<221		DS		· •									·				
<222	2 > 6	25	20														
	_	-	_sig														
<222	2 > 1	124.	.112	9													
			_ 2 &	_													
			_sit														
<222	5> T	141.	.115	ے													
-400	0> 7	Λ															•
ccto	us /	gar 3	ttga	atat	tt c	ccca	ccto	a go	taad	cagt	c ca	tgtg	ggtg	ati	tca	gctct	60
or at	ta a	oa t	at a	itt t	tc c	ag a	gc a	aca g	gta 9	gac a	aaa	tgt	ata	ttc	29	ig aca	109
Me	et G	ly C	ys V	al P	he G	ln S	er :	Thr \	Jal Z	Asp :	Lys	Cys	Ile	Phe	ГУ	s iie	
1		_		5	,					10					15		
gac	tgg	act	ctg	tca	cca	gga	gag	g cad	gc	c aa	g ga	c ga	a ta	it g	tg	cta	157
Asp	Trp	Thr	Leu	Ser	Pro	Gly	Gl:	u His	s Ala	а Lу	s As	p Gl	u Ty	r V	al	Leu	
			20					25					3 (				205
tac	tat	tac	tcc	aat	cto	: agt	gt	g cci	t at	t gg	g cg	C TT	C Ca	ig a	ac 	cgc	205
Tyr	Туз		Ser	Ası	ı Lev	ı Ser		l Pro	0 11	e GI	у аг	g Pr	1e G.	ln A	511	AIG	
		35					40					45			+0	ctc	253
gta	cad	ttg	ato	999	gad	ato		a tg u Cy	c aa	r ya	2 99 2 61	17 Se	2 T.4	-11 T	en	Leu	
Val		Le	ı met	GI	ASI	55 55	פת ב	u Cy	o Ao	II Wa	60	. y 1	-1 -0		-		
	50							g gg	a ac	c ta			at a	aa a	tc	cac	301
caa	yaı	L gr	ים כמני זרט ז	a gas	י אפי פ	. yat	o Gl	n Gl	v Th	r Tv	r Il	le C	ys G	lu I	le	Arg	
65	. AS	.۷۵ ب	. 611		70	- 40)			,	75		٠.		_		80	
C+ C	: פפ	9 00	g gag	g ace		a ato	a tt	c aa	g aa	ggo	g gt	g gi	ta c	tg c	at	gtg	349
Tien	I.V	2 GJ.	y Gli	u Sei	r Gl	n Va	l Ph	e Ly	s Ly	s Al	ā Va	al V	al L	eu F	lis	Val	
				85					90	1				2	95		
ctt	c cc	a qa	g da	a cc	c aa	a ga	g ct	c at	g gt	c ca	it gt	tg g	gt g	ga t	tg	att	397
Lev	ı Pr	o Gl	u Gl	u Pr	o Ly	s Gl	u Le	u Me	t Va	l Hi	s Va	al G	ly G	ly I	.eu	Ile	
			10	0				10	5				1	10			=
cag	g at	g gg	a tg	t gt	t tt	c ca	g ag	c ac	a ga	a gt	g a	aa c	ac g	tg a	acc	aag	445
-			_														

WO 99/31236 -54 - PCT/IB98/02122.

Gln Met Gly Cys Val Phe Gln Ser Thr Glu Val Lys His Val Thr Lys	
115 120 125 gta gaa tgg ata ttt tca gga cgg cgc gca aag gta aca agg agg aaa	493
Val Glu Trp Ile Phe Ser Gly Arg Arg Ala Lys Val Thr Arg Arg Lys 130 135 140	
cat cac tgt gtt aga gaa ggc tct ggc tgatggtatc aggacaaagg	540
His His Cys Val Arg Glu Gly Ser Gly 145 150	
tagaatcagg cacatgagga ggtgttgcaa gagcctgggc tttggtgctt atcagaactg	600
gacettetee tageaattte agetttetgg tgggaaaggt aacteeaatg aagaacaaga acaagaagat gatgatgatg ettaaetttt tggatgeega tatgagattg tacatgtaaa	660 720
gcattttgta taagacttgg cccctgcatt ttagtttcct tctttctccc ttttccttcg	780
tatagagtcc atgggagaat gagggagatg atttttgtgg cccagccaag aaagcaatgg	840
gctagacatt aaaatgatta cacttttatt cttactgggg ttagttctgt gagttttcat	900 960
ctgtgcccca ttgccccatt tatgtgatgg agggaatttt catgggtact tcacgtgttg ggattgattg atcctggggg ccagggtgaa gggtatttta cgggacctct ataaagcagg	1020
aagaagcaag tttattcttt agaccagtag ctctcaacca tgatgtggtc atatatttat	1080
gggtcaacat gtgttgtggg gatatcccaa gtaacttgtt attaataaaa gttaagttgc	1140
aaaaaaaaa aaa	1153
	•
<210> 75	
<212> DNA	
<213> Homo sapiens	
.220	
<220> <221> CDS	
<222> 21167	
400 85	
<400> 75	
ctctqaaatq cttqtctttt atq ctq qna qqt qac cat aqq qct ctq ctt tta	53
ctctgaaatg cttgtctttt atg ctg gna ggt gac cat agg gct ctg ctt tta Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu	53
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10	
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca	53
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10	
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca  Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct	
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro	101
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca  Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct	101
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys	101
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45	101 149 197
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys	101
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat	101 149 197 257 317 377
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta	101 149 197 257 317 377 437
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat	101 149 197 257 317 377
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta	101 149 197 257 317 377 437 497
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10 aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25 ggg aga tta gtg gtg atg gag agg agg gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40 tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45 cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt accatatgtt cacagtacag gatctgtaca taaaagttc tttctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaatttc ttattgctta gaaaattgtc ctccttgtta ttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtcttt tatgctgga ggtgaccata gggctctgct tttaaagata tggctgctc aaaggccaga gtcacaggaa ggacttcttc cagggagatt agtggtgatg gagaggagag	101 149 197 257 317 377 437 497 557 617 677
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaatttc ttattgctta gaaaattgtc ctccttgtta tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtcttt tatgctggga ggtgaccata gggctctgct tttaaagata tggctgcttc aaaggccaga gtcacaggaa ggactcttc cagggagatt agtggtgatg gagaggagag	101 149 197 257 317 377 437 497 557 617 677 737
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu lange at a tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro logg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40 tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45 cacactgga accactagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagt cattaaaaa agatatctat ttgaaagttc tcagagtgt acatatgttt cacagtacag gatctgtaca taaaagttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaatttc ttattgctta gaaaattgtc ctcttgtta ttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtctt tatgctgga ggtgaccata gggctctgct tttaaagata tggctgctc aaaggccaga gtcacaggaa ggacttcttc cagggagatt agtggtgatg gagaggagag	101 149 197 257 317 377 437 497 557 617 677
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu  1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaatttc ttattgctta gaaaattgtc ctccttgtta tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtcttt tatgctggga ggtgaccata gggctctgct tttaaagata tggctgcttc aaaggccaga gtcacaggaa ggactcttc cagggagatt agtggtgatg gagaggagag	101 149 197 257 317 377 437 497 557 617 677 737 797 857 917
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10 aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 20 25 ggg aga tta gtg gtg atg gag agg agg gtt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40 tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45 cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttcctaaac cattcacaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta ttctgtttt taggtgga ggtgaccata gggctctgct tttaaagga agccaatat ggtgtttt tagetgga ggtgaccata gggctctct cagggagtt agtggatgg tcttaaagga agcaacgct cctctgaaat gcttgtctt tatgctgga ggtgaccata gggctctgct tttaaagga tcacaggaa ggactcttc cagggagtt agttgttcac ctcttaatgc aagggccaga ccactaggac cacttaggat gtgatcact tcaggagtgg caagaggagag ttaaaatgac ctcatgcac tctttgcac ggttttgtg agttttcact cttctaatgc aagggtctca cactggaac cacttaggat gtgatcact tcaggtggc aggaatgttgac atatgtttc cagtacaga cacttaggat gtgatcact tcagagtgc aggaatgttgac atatgtttc cagtacaga tctgtacata aaagtttctt tcctaaacca ttcaccaaga gccaatatct aggcattttc ttggtagca aaattttctt attgcttaga aaattgcct ccttgttatt tctgtttgta agacttaat tcgttagaa aaattgtcct tcctgttaat tctgtttgta agacttatct tcctaaacca ttcaccaaga gccaatatct aggcattttc ttggtagcac aaattttctt attgcttaga aaattgcct ccttgttatt tctgtttgta agacttaagt gagagaaa gccaatacca ttcaccaaga gccaatatct aggcattttc ttggtagcac aaattttctt attgcttaga aaattgcct ccttgttatt tctgtttgta agacttaagt gagagaga gccaatacc attcaccaaga gccaatacc attcaccaaga gccaatacc aggcattttc ttggtagcac aaattttctt attaggaaa gccaacgctcc	101 149 197 257 317 377 437 497 557 617 677 797 857 917
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg agg agt taaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagtttc tttctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaattttc ttattgctta gaaaattgtc ctccttgtta ttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtctt tatgctgga ggtgaccata gggctctgct ttaaagata tggctgctc aaaggccaga gtcacaggaa ggactcttc cagggagatt agtggtatg gagaggagg ttaaaatgac ctcatgtcat tcttgtcac ggttttgttg agtttcact cttctaatgc aaggctctca cactgtgaac cacttaggat gtgatcactt tcaggtggc aggaggagg ttaaaatgac ctcatgtcat tcttgtcac ggttttgttg agttttcact cttctaatgc aaggctctca cactgtgaac cacttaggat gtgatcactt tcaggtggc aggatgttg acatagtttg gccagttca tttaaaaaag atactattt gaaagttctc aggattgtac atatgtttc cagtacagga tctgtacata aaagtttct tcctaaacca ttcaccaaga gccaatatct aggcattttc tttgtaacaa aaatttctt tattagctaga aaattgtcc ccttgttatt tctgtttga agacttaatt tctgtaaacaa cacttaaga tctgtacata aaagttcct tcctaaacaa gccaatatct aggcattttc tttgtaacaa aaatttctt tattagctaga aaattgcct ccttgttatt tctgtttga agacttaagt gagttaggtc tttaaggaaa gcaacgctcc ccttgttatt tctgtttga agacttaagt gagttaggtc tttaaggaaa gcaacgctcc tctgtaaatgc ttgtctttna tgctggagg tgaccatagg cccttgcttt taaaggaaa gcaacgctcc tctgtaaatgc ttgtctttna tgctggagg tgaccatagg cccttgcttt taaaggaaa gcaacgctcc tctgtaaatgc ttgtctttna tgctggagg tgaccataagg cccttgcttt taaaggaaa gcaacgctcc tctgaaatgc ttgtctttna tgctggagg tgaccataagg cccttgcttt taaaggaaa gcaacgctcc tctgaaatgc ttgtctttna tgctggaggg tgaccataagg cccttgcttt taaaggaaa gcaacgctcc	101 149 197 257 317 377 437 497 557 617 677 737 797 857 917 977
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg aga gtt aaa atg acc tca tgt cct Gly Arg Leu Val Wal Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagt cattaaaaa agatatctat ttgaaagttc tcagagttgt acatatgtt cacagtacag gatctgtaca taaaagttc tttcctaaac cattcaccaa gagccaatat ctaggcattt tcttggtagc acaaatttc ttattgctta gaaaattgc ctccttgtta ttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtctt tatgctgga ggtgaccata gggctctgct taaaagata tggctgctc aaaggccaga gtcacaggaa ggactcttc cagggagatt agtggtgatg gagaggagag	101 149 197 257 317 377 437 497 557 617 677 797 857 917
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctc cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro  15 20 25  ggg aga tta gtg gtg atg gag agg agg agt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro  30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys  45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggctcagtt catttaaaaa agatatctat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagttc tttcctaaac cattcaccaa gagccaatat tttctgtttg taagacttaa gtggattagg tctttaagga aagcaacgct cctctgtta tttctgtttg taagacttaa gtggattagg tctttaagga aagcaacgct cctctgtaa gcttgtcttt tatgctgga ggtgaccata gggctctgct ttaaaagata tggctgcttc aaaggccaga gtcacaggaa ggacttcttc cagggagatt agtggtgatg gagaggagg ttaaaatagac ctcatgtcct tcttgtccac ggttttgtg agttttcact cttctaatgc aagggtctca cactggaac cacttaggat ggtgaccatt tcaggtggcc aggaatgttg aatgtctttg gctcagttca tttaaaaaaa aaattttct taatgctggc aggatgttga aatgtctttg gctcagttca tttaaaaaaa aatatctatt tcagaagttc cacttaaga gccaatatct aggcatttc ttggtagca aaattttct tatgcttaga aaattgtcc ccttgttatt tctgtttga agacttaaag gtgatcactt tccagaagaa gcaacgctc ccttgttatt tctgtttga agacttaaag gagttaggtc tttaaaggaa gcaacgctc ccttgttatt tctgtttga agacttaaag gagttaggtc ttaaaggaa gcaacgctc ccttgttatt tctgtttga agacttaaag gagttaggtc ttaaaggaa gcaacgctc ccttgttatt tctgtttga agacttaaag gagttaggtc ttaaaggaa gcaacgctc ccttgtaat tctgtttga agactaaag gacttcttcca gggagattag tggtgatgga gaggagagt aaaatgacct catgccttc ttggccacg tttgttga gttttcact tctaatgca aggccagagt cacaggaag acttcttcca gggagattag tggtgatgga gaggagagtt aaaatgacct catgccctc tttgccacg ttttgttga gttttcactct tctaatgcaa gggccagagt cacagaag cctcgccttc ttggccacg ttttgttga gttttcactct tctaatgcaa gggccaaag	101 149 197 257 317 377 437 497 557 617 677 737 797 857 917 977 1037 1097 1157
Met Leu Xaa Gly Asp His Arg Ala Leu Leu Leu 1 5 10  aag ata tgg ctg ctt caa agg cca gag tca cag gaa gga ctt ctt cca Lys Ile Trp Leu Leu Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro 15 20 25  ggg aga tta gtg gtg atg gag agg agg agt aaa atg acc tca tgt cct Gly Arg Leu Val Val Met Glu Arg Arg Val Lys Met Thr Ser Cys Pro 30 35 40  tct tgt cca cgg ttt tgt tgagttttca ctcttctaat gcaagggtct Ser Cys Pro Arg Phe Cys 45  cacactgtga accacttagg atgtgatcac tttcaggtgg ccaggaatgt tgaatgtctt tggetcagtt catttaaaaa agatatcat ttgaaagttc tcagagttgt acatatgttt cacagtacag gatctgtaca taaaagttc tttcctaaac cattcacaa gagccaatat ctaggcattt tcttggtagc acaaatttc ttattgctta gaaaattgtc ctccttgtta tttctgtttg taagacttaa gtgagttagg tctttaagga aagcaacgct cctctgaaat gcttgtcttt tatgctggaa ggagcacata gggctctgct ttaaagaa tgggtgctc aaaggccaga gtcacaggaa ggacttctc cagggagatt agtggtgatg gagaggagg ttaaaatgac ctcatgtcct tcttgccac ggttttgttg agttttcact cttctaatgc aagggtctca cactgtgaac cacttaggat gtgatcactt tcaggtggc aggaatgtg aatgtctttg gctcagtca tttaaaaaag atatctatt gaaagttcc agagttgtac atatgtttc cagtacagga tctgtacata aaagttctt tcctaaacca ttcaccaag gccaatatc aggcatttc ttggtagca aaatttct tctaaagaa acattctc ctcttaatgc atatgtttca cagtacagga tctgtacata aaagttctt tcctaaacca ttcaccaaga gccaatatct aggcatttc ttggtagca aaatttct tataagaaa gcaacgccc ccttgtaat tctgttgta agacttaag gggtaggcc tttaaaggaa gcaacgccc ccttgtaaatgc ttgtctttna tgctggagg tgaccatagg cctctctct taaagaaa gcaacgccc ccttgaaatgc ttgtctttna tgctgggagg tgaccatagg cctctctct taaagaaa gcaacgccc ccttgaaatgc ttgtctttna tgctgggagg tgaccatagg cctctgctt taaagaaag gcgagaggt aaaatgccc catgccctc ttggcaccatagg cctctctcca cggagattag tggtgatgga gagagaggt aaaatgccc catgtcctc ttggcaccatagg cctcttcca cggagattag tggtgatgga gagagaggt aaaatgcccc catgccccc ttggcaccatagg ccccatagg cctctctcca cggagattag tggtgatgga gagagaggt aaaatgcccc catgccctc ttggcaccatagg cctcttcca cggagattag tggtgatgga gagagagat aaaatgcccc catgccctc ttggcaccatagg cctcttcca cggagattag ttgtcctc	101 149 197 257 317 377 437 497 557 617 677 737 797 917 917 917 1037 1097 1157

agttgtacat atgtttcaca gtacaggatc tgtacataaa agtttctttc ctaaaccatt 1337 caccaagage caatatetag geattteett ggtageacaa attttettat tgettagaaa 1457 attgtcctcc ttgttatttc tgtttgtaag acttaagtga gttaggtctt taaggaaagc 1517 aacgctcctc tgaaatgctt gtcttttatg ctgggaggtg accatagggc tctgctttta <210> 76 <211> 526 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 22..318 <221> sig\_peptide <222> 22..93 <223> Von Heijne matrix score 4.6 seq FFIFCSLNTLLLG/GV <221> polyA\_signal <222> 497..502 <221> polyA\_site <222> 516..526 <400> 76 51 ctgcctgctg cttgctgcac c atg aag tct gcc aag ctg gga ttt ctt cta Met Lys Ser Ala Lys Leu Gly Phe Leu Leu -15 -20 aga ttc ttc atc ttc tgc tca ttg aat acc ctg tta ttg ggt ggt gtt 99 Arg Phe Phe Ile Phe Cys Ser Leu Asn Thr Leu Leu Leu Gly Gly Val -10 aat aaa att gcg gag aag ata tgt gga gac ctc aaa gat ccc tgc aaa 147 Asn Lys Ile Ala Glu Lys Ile Cys Gly Asp Leu Lys Asp Pro Cys Lys 195 ttg gac atg aat ttt gga agc tgc tat gaa gtt cac ttt aga tat ttc Leu Asp Met Asn Phe Gly Ser Cys Tyr Glu Val His Phe Arg Tyr Phe 25 20 243 tac aac aga acc tcc aaa aga tgt gaa act ttt gtc ttc tcc ggc tgt Tyr Asn Arg Thr Ser Lys Arg Cys Glu Thr Phe Val Phe Ser Gly Cys 40 45 35 291 aat ggc aac ctt aac aac ttc aag ctt aaa ata gaa cgt gaa gta gcc Asn Gly Asn Leu Asn Asn Phe Lys Leu Lys Ile Glu Arg Glu Val Ala 55 60 338 tgt gtt gca aaa tac aaa cca ccg agg tgagaggatg tgaactcatg Cys Val Ala Lys Tyr Lys Pro Pro Arg 70 aagttgtctg ctgcaccatc cgaaataaag acacaagaaa attcagactg attttgaaat 398 ctttgtaata tttccataat gctttaagct tccatatgtt tgctattttc ctgaccctag 458 ttttgtcttt cctggaaatt aactgtatga tcattagaat gaaagagtct ttctgtcaaa 518 526

<210> 77 <211> 352 <212> DNA <213> Homo sapiens

aaaaaaa

1.

97

145

193

241

289

342

352

55

<220> <221> CDS <222> 8..292 <221> sig peptide <222> 8..118 <223> Von Heijne matrix score 5.6 seg WLLLDALLRLGDT/KK <221> polyA\_signal <222> 317..322 <221> polyA\_site <222> 339..352 ctgagat atg gca agt ccc gct gta aac agg tgg aaa agg cca agg ttg Met Ala Ser Pro Ala Val Asn Arg Trp Lys Arg Pro Arg Leu -35 aag ccg gtg tgg cca cgg cgc ttg gaa tcc tgg ttg ttg ctg gat gct Lys Pro Val Trp Pro Arg Arg Leu Glu Ser Trp Leu Leu Leu Asp Ala -20 -15 ctt ttg cga tta gga gat acc aaa aaa aag cga cag cct gaa gca gcc Leu Leu Arg Leu Gly Asp Thr Lys Lys Lys Arg Gln Pro Glu Ala Ala 1 aca aaa too tgt gtt aga ago ago tgt ggg ggt coo agt gga gat ggg Thr Lys Ser Cys Val Arg Ser Ser Cys Gly Gly Pro Ser Gly Asp Gly 5.0 20 cct ccc cca tgc ctc cag cag cct gac cct cgt gcc ctg tct cag gcg Pro Pro Pro Cys Leu Gln Gln Pro Asp Pro Arg Ala Leu Ser Gln Ala 35 30 ttc tct aga tcc ttt cct ctg ttt ccc tct ctc gct ggc aaa agt atg

Phe Ser Arg Ser Phe Pro Leu Phe Pro Ser Leu Ala Gly Lys Ser Met

atc taattgaaac aagactgaag gatcaataaa cagccatctg ccccttcaaa

50

<210> 78
<211> 542
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 16..378
<221> sig\_peptide
<222> 16..84
<223> Von Heijne matrix score 9.8

Ile

aaaaaaaaa

45 ..

<221> polyA\_signal <222> 502..507

seq FLLFFFLFLLTRG/SL

<221> polyA\_site <222> 522..542

cacgacctgt gggcc atg atg cta ccc caa tgg ctg ctg ctg ttc ctt	
	51
Met Met Leu Pro Gln Trp Leu Leu Leu Phe Leu	
-20 -15	
ctc ttc ttt ctc ttc ctc ctc acc agg ggc tca ctt tct cca aca	99
Leu Phe Phe Leu Phe Leu Leu Thr Arg Gly Ser Leu Ser Pro Thr	
-10 -5 1 5	3.47
aaa tat aac ctt ttg gag ctc aag gag tct tgc atc cgg aac cag gac	147
Lys Tyr Asn Leu Leu Glu Leu Lys Glu Ser Cys Ile Arg Asn Gln Asp	•
10 15 20 tgc gag act ggc tgc tgc caa cgt gct cca gac aat tgc gag tcg cac	195
Cys Glu Thr Gly Cys Cys Gln Arg Ala Pro Asp Asn Cys Glu Ser His	133
25 30 35	
tgc gcg gag aag ggg tcc gag ggc agt ctg tgt caa acg cag gtg ttc	243
Cys Ala Glu Lys Gly Ser Glu Gly Ser Leu Cys Gln Thr Gln Val Phe	
40 45 50	
ttt ggc caa tat aga gcg tgt ccc tgc ctg cgg aac ctg act tgt ata	291
Phe Gly Gln Tyr Arg Ala Cys Pro Cys Leu Arg Asn Leu Thr Cys Ile	
55 60 65	. •
tat toa aag aat gag aaa tgg ott ago ato goo tat ggo ogt tgt cag	339
Tyr Ser Lys Asn Glu Lys Trp Leu Ser Ile Ala Tyr Gly Arg Cys Gln	
70 75 80 85	
aaa att gga agg cag aag ttg gct aag aaa atg ttc ttc tagtgctccc	388
Lys Ile Gly Arg Gln Lys Leu Ala Lys Lys Met Phe Phe	
90 95	
teettettge tgeeteetee teeteeacet geteteetee etaeceagag etetgtgtte	448
accetytice ccagageete caccatgagt ggagggaagt ggggagtgat tgaaataaag	508
agctttttca atgaaaaaaa aaaaaaaaa aaaa	542
<210> 79	
<211> 233	
<211> 233 <212> DNA	
<211> 233 <212> DNA <213> Homo sapiens	
<212> DNA	
<212> DNA	
<212> DNA <213> Homo sapiens	
<212> DNA <213> Homo sapiens <220>	e
<212> DNA <213> Homo sapiens <220> <221> CDS	·
<212> DNA <213> Homo sapiens <220> <221> CDS	, e
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 57233	
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 57233  <400> 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtetttt cttcag atg Met	
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 57233  <400> 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtctttt cttcag atg Met 1	
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 57233  <400> 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtctttt cttcag atg	.· 59
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 57233  &lt;400&gt; 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtcttttt cttcag atg</pre>	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 57233  &lt;400&gt; 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtcttttt cttcag atg</pre>	107
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 57233  &lt;400&gt; 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtcttttt cttcag atg</pre>	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 57233  &lt;400&gt; 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtcttttt cttcag atg</pre>	107
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 57233  &lt;400&gt; 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtcttttt cttcag atg</pre>	107 155
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 57233  &lt;400&gt; 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtcttttt cttcag atg</pre>	107
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 57233  &lt;400&gt; 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtcttttt cttcag atg</pre>	107 155
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 57233  &lt;400&gt; 79 gcaaaaccaa aaccagcacc gatcccgaca tagatcagtg acgtcttttt cttcag atg</pre>	107 155

<210> 80 <211> 660

50

Pro Arg Lys Arg Glu Gly Lys Lys Lys

55

<212> DNA

<213> Homo sapiens <220> <221> CDS <222> 83..340 <221> sig\_peptide <222> 83..124 <223> Von Heijne matrix score 7.5 seq VALNLILVPCCAA/WC <221> polyA\_signal <222> 573..578 <221> polyA\_site <222> 607..660 <400> 80 60 qaatttgtaa aacttctgct cgtttacact gcacattgaa tacaggtaac taattggaag gagagggag atcactcttt tg atg gtg gcc ctg aac ctc att ctg gtt ccc 112 Met Val Ala Leu Asn Leu Ile Leu Val Pro -10 tgc tgc gct gct tgg tgt gac cca cgg agg atc cac tcc cag gat gac. 160 Cys Cys Ala Ala Trp Cys Asp Pro Arg Ile His Ser Gln Asp Asp 208 gtg ccc cgt agc tct gct gct gat act ggg tct gcg atg cag cgg cgt Val Pro Arg Ser Ser Ala Ala Asp Thr Gly Ser Ala Met Gln Arg Arg 20 15 25 256 gag gcc tgg gct ggt tgg aga agg tca caa ccc ttc tct gtt ggt ctg Glu Ala Trp Ala Gly Trp Arg Arg Ser Gln Pro Phe Ser Val Gly Leu .35 304 cct tct gct gaa aga ctc gag aac caa cca ggg aag ctg tcc tgg agg Pro Ser Ala Glu Arg Leu Glu Asn Gln Pro Gly Lys Leu Ser Trp Arg 50 55 45 tcc ctg gtc gga gag gga tat aga atc tgt gac ctc tgacaactgt 350 Ser Leu Val Gly Glu Gly Tyr Arg Ile Cys Asp Leu gaagccaccc tgggctacag aaaccacagt cttcccagca attattacaa ttcttgaatt 410 ccttggggat tttttactgc cctttcaaag cacttaagtg ttagatctaa cgtgttccag 470 tgtctgtctg aggtgactta aaaaatcaga acaaaacttc tattatccag agtcatggga 530 gagtacaccc tttccaggaa taatgttttg ggaaacactg aaatgaaatc ttcccagtat 590 650 tataaattgt gtatttaaaa aaagaaactt ttctgaatgc ctacctggcg gtgtatacca 660 ggcagtgtgc

<210> 81 <211> 605

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 47..541

<221> sig\_peptide

<222> 47..220

<223> Von Heijne matrix
 score 5.4
 seq QLLDSVLWLGALG/LT

<221> polyA\_site <222> 597..605"

<400	> 81								•								
												M	let I	cc c	ırg		55
ctc	tgc	tta	ccc	aga	ccc	gaa	gca -	cgt	gag	gat	ccg	atc	cca	gtt	cct		103
Leu	Сув	Leu	Pro	Arg		Glu	Ala	Arg	Glu		Pro	Ile	Pro	Val			
-55					-50					-45					-40		
cca	agg	ggc	ctg	ggt	gct	999	gag	999	tca	ggt	agt	сса	gtg	cgt	cca		151
Pro	Arg	Gly	Leu		Ala	Gly	Glu	Gly		Gly	Ser	Pro	Val	Arg	Pro		
				-35					-30					-25			
														agt			199
Pro	Val	Ser		Trp	Glŷ	Pro	Ser		Ala	Gln	Leu	Leu		Ser	Val		
			-20					-15					-10				
cta	tgg	ctg	999	gca	cta	gga	ctg	aca	atc	cag	gca	gtc	ttt	tcc	acc		247
Leu	Trp		Gly	Ala	Leu	Gly	Leu	Thr	Ile	Gin		Val	Phe	Ser	Tnr		
		-5					1				5	_					
act	ggc	cca	gcc	ctg	ctg	ctg	ctt	ctg	gtc	agc	ttc	ctc	acc	ttt	gac	•;	295
Thr	Gly	Pro	Ala	Leu		Leu	Leu	Leu	Val		Phe	Leu	Thr	Phe			
10				•	15					20					25		
														ctt			343
Leu	Leu	His	Arg		Ala	Gly	His	Thr		Pro	Gin	Arg	Lys	Leu	Leu		
				30					35					40			
														cag			391
Thr	Arg	Gly		Ser	Gln	Gly	Ala		Glu	GIA	Pro	GIÀ		Gln	Giu		
			45					50			•		55				430
														ctc			439
Ala	Leu		Leu	Gln	Met	Gly		Val	Ser	Gly	GIn		ser	Leu	GIN		•
		60					65					70					402
														aga			487
Asp		Leu	Leu	Leu	Leu		Met	GIÀ	Leu	GIA		Leu	ren	Arg	ATA		
	75					80					85						<b>-</b> 2-
														cat			535
-	Gly	Met	Pro	Leu		Leu	Leu	GIY	Leu		Pne	Cys	ьeu	His			
90					95					100		_ 4	+		105		591
	_	tga	gagc	ccc	tccc.	caca	ac t	cagt	gtcc	t tc	aaat	atac	aat	gacc	acc		221
_	Ala																605
ctt	cttc	aaa	aaaa														000

<210> 82
<211> 396
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 46..285

<221> sig\_peptide
<222> 46..150
<223> Von Heijne matrix
score 3.6
seq LEPGLSSSAACNG/KE

<221> polyA\_signal <222> 364..369

<221> polyA\_site <222> 385..396

ij,

<400> 82 cctctacagg aatcagactc agcctctttt ggttttcagt gaagt atg cct ttt caa Met Pro Phe Gln	<b>5</b> 7
-35  ttt gga acc cag cca agg agg ttt cca gtg gaa gga gga gat tct tca  Phe Gly Thr Gln Pro Arg Arg Phe Pro Val Glu Gly Gly Asp Ser Ser -30 -25 -20	105
att gag ctg gaa cct ggg ctg agc tcc agt gct gcc tgt aat ggg aag  Ile Glu Leu Glu Pro Gly Leu Ser Ser Ala Ala Cys Asn Gly Lys -15 -10 -5 1	153
gag atg tca cca acc agg caa ctc cgg agg tgc cct gga agt cat tgc Glu Met Ser Pro Thr Arg Gln Leu Arg Arg Cys Pro Gly Ser His Cys 5 10 15	201
ctg aca ata act gat gtt ccc gtc act gtt tat gca aca acg aga aag Leu Thr Ile Thr Asp Val Pro Val Thr Val Tyr Ala Thr Thr Arg Lys 20 25 30	249
cca cct gca caa agc agc aag gaa atg cat cct aaa tagcaccatt Pro Pro Ala Gln Ser Ser Lys Glu Met His Pro Lys 35 40 45	295
aagtetttig teaaggietg aetaggieaa ggglaatgga eeagtateat eiggigatet gglaacaaa taaaagiggi ggeaeettea aaaaaaaaaa a	355 396
<210> 83 <211> 432 <212> DNA	
<213> Homo sapiens	
<220> <221> CDS <222> 22240	
<221> sig_peptide <222> 2284	
<223> Von Heijne matrix score 12 seq VLVLCVLLLQAQG/GY	
<221> polyA_signal <222> 397402	
<221> polyA_site <222> 421432	
<pre>&lt;400&gt; 83 gctcacgctc tggtcagagt t atg gca ccc cag act ctg ctg cct gtc ctg</pre>	51
gtt ctc tgt gtg ctg ctg ctg cag gcc cag gga gga tac cgt gac aag Val Leu Cys Val Leu Leu Gln Ala Gln Gly Gly Tyr Arg Asp Lys -10 -5 1 5	99
atg agg atg cag aga atc aag gtc tgt gag aag cga ccc agc ata gat  Met Arg Met Gln Arg Ile Lys Val Cys Glu Lys Arg Pro Ser Ile Asp  10 15 20	147
cta tgc atc cac tgt tca tgt ttc caa aag tgt gaa aca aat aag Leu Cys Ile His His Cys Ser Cys Phe Gln Lys Cys Glu Thr Asn Lys 25 30 35	195
ata tgc tgt tca gcc ttc tgt ggg aac att tgt atg agc atc cta Ile Cys Cys Ser Ala Phe Cys Gly Asn Ile Cys Met Ser Ile Leu 40 45 50	240

tgagtgggag agtgggctgg gatgtgcatc ctgctccctg aacccttcca tccgagactg tgcccacatc cgaagcacaa ggacatcaaa tcatcagcac aagaacatca acaggaatgc caccctcccc agtgtctgaa ctccctgtcc ctgtcaaatg aaccagaaca aatgcccatg	300 360 420
aaaaaaaaa aa	432
<210> 84	
<211> 420	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 89382	
<221> polyA site	
<222> 408420	
400 04	
<pre>&lt;400&gt; 84  GCTTGCCTGB CCCCCBTGTC GCCTCTGTBG GTDGCCCGC Tableton to the control of the control</pre>	
gcttgcctga ccccatgtc gcctctgtag gtagaagaag tatgtcttcc tggaccccct ggctggtgct gtaacaaaga cccatgtg atg ctg ggg gca gag aca gag gag	60 112
Met Leu Gly Ala Glu Thr Glu Glu	112
1 5	
aag ctg ttt gat gcc ccc ttg tcc atc agc aag aga gag cag ctg gaa	160
Lys Leu Phe Asp Ala Pro Leu Ser Ile Ser Lys Arg Glu Gln Leu Glu	
10 15 20 Cag gate cea gag aac tac tte tat gtg cea gae etg gge eag gtg	200
Gln Gln Val Pro Glu Asn Tyr Phe Tyr Val Pro Asp Leu Gly Gln Val	208
25 30 35 40	
CCT dad att dat dtt doe too too dta det and att	
cct gag att gat gtt cca tcc tac ctg cct gac ctg ccc ggc att gcc	256
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala	256
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala 45 50 55	
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala 45 50 55 aac gac ctc atg tac att gcc gac ctg ggc ccc qqc att gcc ccc tct	304
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala 45 50 55	
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala 45 50 55 aac gac ctc atg tac att gcc gac ctg ggc ccc ggc att gcc ccc tct Asn Asp Leu Met Tyr Ile Ala Asp Leu Gly Pro Gly Ile Ala Pro Ser 60 65 70 gcc cct ggc acc att cca gaa ctg ccc acc ttc cac act gag gta gcc	
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala 45  aac gac ctc atg tac att gcc gac ctg ggc ccc ggc att gcc ccc tct  Asn Asp Leu Met Tyr Ile Ala Asp Leu Gly Pro Gly Ile Ala Pro Ser 60  65  70  gcc cct ggc acc att cca gaa ctg ccc acc ttc cac act gag gta gcc  Ala Pro Gly Thr Ile Pro Glu Leu Pro Thr Phe His Thr Glu Val Ala	304
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala 45  aac gac ctc atg tac att gcc gac ctg ggc ccc ggc att gcc ccc tct Asn Asp Leu Met Tyr Ile Ala Asp Leu Gly Pro Gly Ile Ala Pro Ser 60  65  70  gcc cct ggc acc att cca gaa ctg ccc acc ttc cac act gag gta gcc Ala Pro Gly Thr Ile Pro Glu Leu Pro Thr Phe His Thr Glu Val Ala 75  80  85	304 352
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala 45  aac gac ctc atg tac att gcc gac ctg ggc ccc ggc att gcc ccc tct Asn Asp Leu Met Tyr Ile Ala Asp Leu Gly Pro Gly Ile Ala Pro Ser 60  gcc cct ggc acc att cca gaa ctg ccc acc ttc cac act gag gta gcc Ala Pro Gly Thr Ile Pro Glu Leu Pro Thr Phe His Thr Glu Val Ala 75  80  85  gag cct ctc aag acc tac aag atg ggg tac taacaagcacc accaccacc	304
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala 45  aac gac ctc atg tac att gcc gac ctg ggc ccc ggc att gcc ccc tct Asn Asp Leu Met Tyr Ile Ala Asp Leu Gly Pro Gly Ile Ala Pro Ser 60  gcc cct ggc acc att cca gaa ctg ccc acc ttc cac act gag gta gcc Ala Pro Gly Thr Ile Pro Glu Leu Pro Thr Phe His Thr Glu Val Ala 75  80  85  gag cct ctc aag acc tac aag atg ggg tac taacagcacc accaccgccc Glu Pro Leu Lys Thr Tyr Lys Met Gly Tyr	304 352
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala 45  aac gac ctc atg tac att gcc gac ctg ggc ccc ggc att gcc ccc tct Asn Asp Leu Met Tyr Ile Ala Asp Leu Gly Pro Gly Ile Ala Pro Ser 60  gcc cct ggc acc att cca gaa ctg ccc acc ttc cac act gag gta gcc Ala Pro Gly Thr Ile Pro Glu Leu Pro Thr Phe His Thr Glu Val Ala 75  80  85  gag cct ctc aag acc tac aag atg ggg tac taacagcacc accaccgccc Glu Pro Leu Lys Thr Tyr Lys Met Gly Tyr	304 352 :
Pro Glu Ile Asp Val Pro Ser Tyr Leu Pro Asp Leu Pro Gly Ile Ala 45  aac gac ctc atg tac att gcc gac ctg ggc ccc ggc att gcc ccc tct Asn Asp Leu Met Tyr Ile Ala Asp Leu Gly Pro Gly Ile Ala Pro Ser 60  gcc cct ggc acc att cca gaa ctg ccc acc ttc cac act gag gta gcc Ala Pro Gly Thr Ile Pro Glu Leu Pro Thr Phe His Thr Glu Val Ala 75  80  85  gag cct ctc aag acc tac aag atg ggg tac taacagcacc accaccgccc Glu Pro Leu Lys Thr Tyr Lys Met Gly Tyr 90	304 352

<210> 85

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 80..415

<221> sig\_peptide

<222> 80..142

<223> Von Heijne matrix score 5.4 seq TFCLIFGLGAVWG/LG

<221> polyA\_signal

WO 99/31236 -62- PCT/IB98/02122

<222> 471..476 W <221> polyA\_site <222> 488..501 <400> 85 60 cccgcttgat tccaagaacc tcttcgatat ttatttttat ttttaaagag ggagacgatg gactgagetg atcegeace atg gag tet egg gte tta etg aga aca tte tgt 112 Met Glu Ser Arg Val Leu Leu Arg Thr Phe Cys -20 -15 160 ttg atc ttc ggt ctc gga gca gtt tgg ggg ctt ggt gtg gac cct tcc Leu Ile Phe Gly Leu Gly Ala Val Trp Gly Leu Gly Val Asp Pro Ser -5 cta cag att gac gtc tta aca gag tta gaa ctt ggg gag tcc acg acc 208 Leu Gln Ile Asp Val Leu Thr Glu Leu Glu Leu Gly Glu Ser Thr Thr 10. 256 gga gtg cgt cag gtc ccg ggg ctg cat aat ggg acg aaa gcc ttt ctc Gly Val Arg Gln Val Pro Gly Leu His Asn Gly Thr Lys Ala Phe Leu 30 35 304 ttt caa gat act ccc aga agc ata aaa gca tcc act gct aca gct gaa Phe Gln Asp Thr Pro Arg Ser Ile Lys Ala Ser Thr Ala Thr Ala Glu 45 cag ttt ttt cag aag ctg aga aat aaa cat gaa ttt act att ttg gtg Gln Phe Phe Gln Lys Leu Arg Asn Lys His Glu Phe Thr Ile Leu Val 60 65 400 acc cta aaa cag acc cac tta aat tca gga gtt att ctc tca att cac Thr Leu Lys Gln Thr His Leu Asn Ser Gly Val Ile Leu Ser Ile His 80 75 cac ttg gat cac agg taaatgtggt tgctggagtt tcctgtgttt tcattatatg His Leu Asp His Arg 90 501 tggttaaatg aatatattaa agagaagtaa acaaaaaaaa aaaaaa <210> 86 <211> 454 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 152..361 <221> sig\_peptide <222> 152..283 <223> Von Heijne matrix score 4.7 seg FLLSLSLITYCFW/DP <400> 86 60 gacattttac ttttttctgt taacgcttac cctagaaatt agaaatgaca ccacgtattc ttagcgaagt ccagttttca gcattttgtc cttattggac aatagcaagg atattagaac 120 172 gtgttggttc cgcgtgcttc cgtcttgagt t atg tgc tgc tat tgt cgg ata Met Cys Cys Tyr Cys Arg Ile ttt tgt ctt aga tgt acg tac ttt cct gtt cat tgt ggt atg tgt aat 220 Phe Cys Leu Arg Cys Thr Tyr Phe Pro Val His Cys Gly Met Cys Asn -30 ttg cgt tac ttt gaa ttt tcc acg ttt tta ctt tct ttg tct ctc atc 268

Leu Arg Tyr Phe Glu Phe Ser Thr Phe Leu Leu Ser Leu Ser Leu Ile

-63-WO 99/31236 PCT/IB98/02122 -

act tac tgc ttt tgg gac ccc ccc cat cgg ggt tca cat tcc ctc tcc Thr Tyr Cys Phe Trp Asp Pro Pro His Arg Gly Ser His Ser Leu Ser -5 1 5 10	316
cta gag cac act ccc ttg gat ttc ctc gag tgg ggt ctg ctg cgg Leu Glu His Thr Pro Leu Asp Phe Leu Glu Trp Gly Leu Leu Arg 15 20 25	361
tgaagctttc ccattttatg tgcagattat tttcagaggg tatatagaat tcaggcagct	421 454
<210> 87	
<211> 1272 <212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 32307	•
<221> sig_peptide	
<222> 3270	
<pre>&lt;223&gt; Von Heijne matrix score 4.2</pre>	
seq MLFSLSLLSNLNQ/IG	
<221> polyA_signal	
	•
<221> polyA_site <222> 12611272	
(222) 12611272	
.400- 00	
<400> 87	
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt	52
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt Met Leu Phe Ser Leu Ser Leu -10	52
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac	52 100
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt Met Leu Phe Ser Leu Ser Leu -10	
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5  1  5  10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa	
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5  1  5  10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gln	100
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5  1  5  10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gln  15  20  25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc cac	100
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gln  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc cac Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile His	100 148
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5	100 148 196
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5	100 148
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5	100 148 196
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gln  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc cac Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile His  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aaa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Lys  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tca	100 148 196
Met Leu Phe Ser Leu Ser Leu  Met Leu Phe Ser Leu Ser Leu  10  Ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gln  15 20 25  Caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc cac Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile His  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aaa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Lys  45 50 55  Cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tca Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Ser  60 65	100 148 196
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5	100 148 196
Met Leu Phe Ser Leu Ser Leu  Met Leu Phe Ser Leu Ser Leu  10  Ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gln  15 20 25  Caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc cac Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile His  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aaa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Lys  45 50 55  Cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tca Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Ser  60 65	100 148 196 244
Met Leu Phe Ser Leu Ser Leu  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5 1 5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gln  15 20 25  caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc cac Gln Leu Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile His  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aaa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Lys  45 50  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tca Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Ser  60 65 70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aagcttctct Pro Phe Leu Ala Cys 75  cgcagccgga gcaggtccct ttctagagat aggagaagag agagatcgct gtctcgggag	100 148 196 244
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5	100 148 196 244 292 347 407 467
gtcaggttgc accgcccttt ggttcccgag c atg ctg ttt tct ctc agc ctt  Met Leu Phe Ser Leu Ser Leu  -10  ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5	100 148 196 244 292 347 407 467 527
Met Leu Phe Ser Leu Ser Leu  Met Leu Phe Ser Leu Ser Leu  10  Ctc tcc aac ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  5 10  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gln  15 20 25  Caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc cac Gln Leu Gln Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile His  30 35 40  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aaa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Lys  45 50 55  cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tca Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Ser  60 65 70  cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aggattctct Pro Phe Leu Ala Cys 75  Cgcagccgga gcaggtccct ttctagagat aggagaagag agagatcgct gtctcggag agaaatcaca agccgtcccg atccttctct aggtctcgta gtcgatttag gtcaaatgaa aggaaataga agacagtttg caagagaagt ggtgtacagg aaattacttc atttgacagg agtatgtaca gaaaattcaa gttttgtttg agacttcata agcttggtgc atttttaaga	100 148 196 244 292 347 407 467 527 587
Met Leu Phe Ser Leu Ser Leu  Met Leu Phe Ser Leu Ser Leu  -10  Ctc tcc aac Ctt aac caa atc ggc agc agc cac ctc gac cgc cca cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5  1  att cct ggc caa tca gct cag ctg ttt att tac caa atg tct tca caa Ile Pro Gly Gln Ser Ala Gln Leu Phe Ile Tyr Gln Met Ser Ser Gln  15  20  25  Caa cta cag cag cag cct tcg gct aac aaa aaa gca gga aaa atc cac Gln Leu Gln Gln Pro Ser Ala Asn Lys Lys Ala Gly Lys Ile His  30  aac acc ccc ttc gcc aac caa cta aat cca acg caa cat ctg gca aaa Asn Thr Pro Phe Ala Asn Gln Leu Asn Pro Thr Gln His Leu Ala Lys  45  50  55  Cct ttt cag caa att ctt cct ggc cgt cag tcc ggc agc ctc acc tca Pro Phe Gln Gln Ile Leu Pro Gly Arg Gln Ser Gly Ser Leu Thr Ser  60  65  70  Cca ttt cta gct tgc tgaaacccaa aactaatctc caagaaggag aggatcgct gtctcgggag agaaatcaca agccgtccc atccttctct aggtctcgta gtcgatttag gtcaaatgaa aggaaatcaca agcagttcc caagaaggag ggtgtccaag aactactca agcttgtgc attttaaga tgttttagct gtcaaaatc gtttgtttg agactccata accaagaatgttact tacaaatgttc atggtttgaa atggatcata cgaggcatgt aataaccaaga attgttactt tacaatttc catgggtttgaa atggatcata cgaggcatgt aataaccaaga attgttactt tacaattttc catgggtttgaa atggatcata cgaggcatgt aataaccaaga attgttactt tacaattttc atggtttgaa atggatcata cgaggcatgt aataaccaaga attgttactt tacaattttc atgggtttgaa atggatcata cgaggcatgt aataaccaaga attacttt tacaattttc atgggtttgaa attggatcata cgaggcatgt gtacaattcct atagacaaga attacaacaaga attacaacaaga attacaacaacaacaacaacaacaacaacaacaacaacaa	100 148 196 244 292 347 407 467 527
Steagstige accepted gettecegas c atg ctg tit tet etc age ett  Met Leu Phe Ser Leu Ser Leu  -10  Ctc tec aac ett aac caa ate gge age age cac ete gac ege cac cac Leu Ser Asn Leu Asn Gln Ile Gly Ser Ser His Leu Asp Arg Pro His  -5	100 148 196 244 292 347 407 467 527 587 647

WO 99/31236 -64- PCT/IB98/02122

aaattgaact aagatttact tttttttccaaacagcagt ctttaaaaac tgctgtgaacactattaaat tagaggtttt tgaaaaactctggtatagaa tgttaagttt caagaaagttttgattgccg tatatggata catggctgtttcaaaaatg tcctgccagt ttaagggtacaagattttt ttcatgctgt catttgtaactttggttaca gattaaaaaa aaaaa	a cacaggecat c aacteteate t tacetttget c cgtgacatte c attgtagage	caggaaaac gaaatgctgc ctgggcagag gttgcctagt ttaggtcgta agttccttat tttatgtgca aatttgtgat cgaactttga gttactgtgc	947 1007 1067 1127 1187
		•	
<210> 88	•		
<211> 804			•
<212> DNA <213> Homo sapiens		d	•
(213) Nomo Sapiens		•	
<220>			
<221> CDS <222> 114734			•
	•		
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 114239</pre>			•
<223> Von Heijne matrix	ı	•	•
score 5.2			
seq LLFDLVCHEFCQS/DD			
<221> polyA_signal			
<222> 768773		•	
<221> polyA_site <222> 793804		•	
<400> 88			
ccaacaccag gaagagtetg aagagcage			
ccaacaccag gaagagtetg aagagcage agetgecaaa caagtaeggt agttetgaa			60 116
agctgccaaa caagtacggt agttctgaa cac att tta caa ctg ctt act aca	a atccagaatg gtg gat gat	gcttgatgtt tac atg Met gga att caa gca att	
agctgccaaa caagtacggt agttctgaa	a atccagaatg gtg gat gat	g gcttgatgtt tac atg Met gga att caa gca att Gly Ile Gln Ala Ile	116
agctgccaaa caagtacggt agttctgaa cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35 gta cat tgt cct gac act gga aaa	a atccagaatg gtg gat gat Val Asp Asp gac att tgg	g gcttgatgtt tac atg Met gga att caa gca att Gly Ile Gln Ala Ile -30 g aat tta ctt ttt gac	116
agctgccaaa caagtacggt agttctgaa cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35 gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys	a atccagaatg gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp	g gcttgatgtt tac atg Met gga att caa gca att Gly Ile Gln Ala Ile -30 g aat tta ctt ttt gac Asn Leu Leu Phe Asp	116
agctgccaaa caagtacggt agttctgaa cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35 gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 -20	a atccagaatg gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15	g gcttgatgtt tac atg Met  gga att caa gca att Gly Ile Gln Ala Ile -30 g aat tta ctt ttt gac Asn Leu Leu Phe Asp -10	116
agctgccaaa caagtacggt agttctgaa  cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35  gta cat tgt cct gac act gga aaa  Val His Cys Pro Asp Thr Gly Lys -25 -20  ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat	Met  Met  Gga att caa gca att  Gly Ile Gln Ala Ile  -30  g aat tta ctt ttt gac  Asn Leu Leu Phe Asp  -10  Cca ccc atc att ctt  Pro Pro Ile Ile Leu	116 164 212
agctgccaaa caagtacggt agttctgaa  cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35  gta cat tgt cct gac act gga aaa  Val His Cys Pro Asp Thr Gly Lys -25 -20  ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp	Met  Met  Gga att caa gca att  Gly Ile Gln Ala Ile  -30  g aat tta ctt ttt gac  Asn Leu Leu Phe Asp  -10  Cca ccc atc att ctt  Pro Pro Ile Ile Leu  5	116 164 212 260
agctgccaaa caagtacggt agttctgaa  cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35  gta cat tgt cct gac act gga aaa  Val His Cys Pro Asp Thr Gly Lys -25 -20  ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt	Met  Met  Gga att caa gca att  Gly Ile Gln Ala Ile  -30  g aat tta ctt ttt gac  Asn Leu Leu Phe Asp  -10  Cca ccc atc att ctt  Pro Pro Ile Ile Leu  5  tca gtg ttg tct gcc	116 164 212
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35  gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 -20 ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5 caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 15	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe	Met  Gga att caa gca att  Gly Ile Gln Ala Ile  -30  g aat tta ctt ttt gac  Asn Leu Leu Phe Asp  Cca ccc atc att ctt  Pro Pro Ile Ile Leu  5  t tca gtg ttg tct gcc  Ser Val Leu Ser Ala  20	116 164 212 260 308
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35 gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 -20 ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5 caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 15 atc tat gcc tca cag act gag caa	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe	Met  Gga att caa gca att  Gly Ile Gln Ala Ile  -30  g aat tta ctt ttt gac  Asn Leu Leu Phe Asp  Cca ccc atc att ctt  Pro Pro Ile Ile Leu  5  t tca gtg ttg tct gcc  Ser Val Leu Ser Ala  20  a aag ata gaa aaa gta	116 164 212 260
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35 gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5 caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 15 atc tat gcc tca cag act gag caa Ile Tyr Ala Ser Gln Thr Glu Gln 25	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe	Met  Gga att caa gca att Gly Ile Gln Ala Ile  -30  g aat tta ctt ttt gac  Asn Leu Leu Phe Asp  Cca ccc atc att ctt Pro Pro Ile Ile Leu  5  t tca gtg ttg tct gcc Ser Val Leu Ser Ala  20  a aag ata gaa aaa gta Lys Ile Glu Lys Val  35	116 164 212 260 308
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35 gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5 caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 15 atc tat gcc tca cag act gag caa Ile Tyr Ala Ser Gln Thr Glu Gln 25 gat ctt cct cta att gac agc ctc	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe gag tat cta Glu Tyr Leu	Met  Gga att caa gca att  Gly Ile Gln Ala Ile  -30  g aat tta ctt ttt gac  Asn Leu Leu Phe Asp  -10  Cca ccc atc att ctt  Pro Pro Ile Ile Leu  5  tca gtg ttg tct gcc  Ser Val Leu Ser Ala  20  a aag ata gaa aaa gta  Lys Ile Glu Lys Val  35  c tta caa aat atg gaa	116 164 212 260 308
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35 gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5 caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 15 atc tat gcc tca cag act gag caa Ile Tyr Ala Ser Gln Thr Glu Gln 25	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe gag tat cta Glu Tyr Leu	Met  Gga att caa gca att  Gly Ile Gln Ala Ile  -30  g aat tta ctt ttt gac  Asn Leu Leu Phe Asp  -10  Cca ccc atc att ctt  Pro Pro Ile Ile Leu  5  tca gtg ttg tct gcc  Ser Val Leu Ser Ala  20  a aag ata gaa aaa gta  Lys Ile Glu Lys Val  35  c tta caa aat atg gaa	116 164 212 260 308
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5 caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 atc tat gcc tca cag act gag caa Ile Tyr Ala Ser Gln Thr Glu Gln 25 gat ctt cct cta att gac agc ctc Asp Leu Pro Leu Ile Asp Ser Leu 40 cag tgt cag aaa aaa cca gag aac	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe gag tat cta Glu Tyr Leu att cgg gtc Ile Arg Val	Met  General Met	116 164 212 260 308
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35  gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 -20  ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5  caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 15  atc tat gcc tca cag act gag caa Ile Tyr Ala Ser Gln Thr Glu Gln 25  gat ctt cct cta att gac agc ctc Asp Leu Pro Leu Ile Asp Ser Leu 40  cag tgt cag aaa aaa cca gag aac Gln Cys Gln Lys Lys Pro Glu Asr	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe gag tat cta Glu Tyr Lev att cgg gtc Ile Arg Val tcg gca gag Ser Ala Glu	Met  Gga att caa gca att  Gly Ile Gln Ala Ile  -30  aat tta ctt ttt gac  Asn Leu Leu Phe Asp  -10  Cca ccc atc att ctt  Pro Pro Ile Ile Leu  5  tca gtg ttg tct gcc  Ser Val Leu Ser Ala  20  a aag ata gaa aaa gta  Lys Ile Glu Lys Val  35  tta caa aat atg gaa  Leu Gln Asn Met Glu  55  tct aac aca gag gaa  1 Ser Asn Thr Glu Glu	116 164 212 260 308 356
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35  gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 -20  ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5  caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 15  atc tat gcc tca cag act gag caa Ile Tyr Ala Ser Gln Thr Glu Gln 25  gat ctt cct cta att gac agc ctc Asp Leu Pro Leu Ile Asp Ser Leu 40 45  cag tgt cag aaa aaa cca gag aac Gln Cys Gln Lys Lys Pro Glu Asp 60  act aaa agg act gat tta acc caa	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe gag tat cta Glu Tyr Lev att cgg gtc Ile Arg Val tcg gca gag Ser Ala Glu 65 gat gat ctc	Met  Gga att caa gca att  Gly Ile Gln Ala Ile  -30  aat tta ctt ttt gac  Asn Leu Leu Phe Asp  -10  cca ccc atc att ctt  Pro Pro Ile Ile Leu  5  tca gtg ttg tct gcc  Ser Val Leu Ser Ala  20  a aag ata gaa aaa gta  Lys Ile Glu Lys Val  35  tta caa aat atg gaa  Leu Gln Asn Met Glu  55  tct aac aca gag gaa  1 Ser Asn Thr Glu Glu  70  cac ttg aaa atc tta	116 164 212 260 308 356
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35  gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 -20  ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5  caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 atc tat gcc tca cag act gag caa Ile Tyr Ala Ser Gln Thr Glu Gln 25 30  gat ctt cct cta att gac agc ctc Asp Leu Pro Leu Ile Asp Ser Leu 40 45  cag tgt cag aaa aaa cca gag aac gal ctg cag tgt cag aaa aaa cca gag aac Gln Cys Gln Lys Lys Pro Glu Asr 60  act aaa agg act gat tta acc caa Thr Lys Arg Thr Asp Leu Thr Glr	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe gag tat cta Glu Tyr Lev att cgg gtc Ile Arg Val tcg gca gac Ser Ala Glu 65 gat gat ctc Asp Asp Lev	Met  Gga att caa gca att  Gly Ile Gln Ala Ile  -30  gaat tta ctt ttt gac  Asn Leu Leu Phe Asp  -10  Cca ccc atc att ctt  Pro Pro Ile Ile Leu  5  tca gtg ttg tct gcc  Ser Val Leu Ser Ala  20  a aag ata gaa aaa gta  Lys Ile Glu Lys Val  35  ctta caa aat atg gaa  Leu Gln Asn Met Glu  55  tct aac aca gag gaa  1 Ser Asn Thr Glu Glu  70  cac ttg aaa atc tta  His Leu Lys Ile Leu	116 164 212 260 308 356 404
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35  gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 -20  ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5  caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 atc tat gcc tca cag act gag caa Ile Tyr Ala Ser Gln Thr Glu Gln 25 30  gat ctt cct cta att gac agc ctc Asp Leu Pro Leu Ile Asp Ser Leu 40  cag tgt cag aaa aaa cca gag aac Gln Cys Gln Lys Lys Pro Glu Asr 60  act aaa agg act gat tta acc cas Thr Lys Arg Thr Asp Leu Thr Glr	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe gag tat cta Glu Tyr Lev att cgg gtc Ile Arg Val att cgg gtc Ile Arg Val ser Ala Glu 65 gat gat ctc Asp Asp Lev 80	Met  gga att caa gca att  Gly Ile Gln Ala Ile  -30  aat tta ctt ttt gac  Asn Leu Leu Phe Asp  -10  cca ccc atc att ctt  Pro Pro Ile Ile Leu  5  tca gtg ttg tct gcc  Ser Val Leu Ser Ala  20  a aag ata gaa aaa gta  Lys Ile Glu Lys Val  35  ctta caa aat atg gaa  Leu Gln Asn Met Glu  55  tct aac aca gag gaa  1 Ser Asn Thr Glu Glu  70  cac ttg aaa atc tta  1 His Leu Lys Ile Leu  85	116 164 212 260 308 356 404 452 500
cac att tta caa ctg ctt act aca His Ile Leu Gln Leu Leu Thr Thr -40 -35  gta cat tgt cct gac act gga aaa Val His Cys Pro Asp Thr Gly Lys -25 -20  ctg gtc tgc cat gaa ttc tgc cag Leu Val Cys His Glu Phe Cys Gln -5  caa gaa cag aaa aca gtg cta gcc Gln Glu Gln Lys Thr Val Leu Ala 10 atc tat gcc tca cag act gag caa Ile Tyr Ala Ser Gln Thr Glu Gln 25 30  gat ctt cct cta att gac agc ctc Asp Leu Pro Leu Ile Asp Ser Leu 40 45  cag tgt cag aaa aaa cca gag aac gal ctg cag tgt cag aaa aaa cca gag aac Gln Cys Gln Lys Lys Pro Glu Asr 60  act aaa agg act gat tta acc caa Thr Lys Arg Thr Asp Leu Thr Glr	gtg gat gat Val Asp Asp gac att tgg Asp Ile Trp -15 tct gat gat Ser Asp Asp 1 tct gtt ttt Ser Val Phe gag tat cta Glu Tyr Lev att cgg gtc Ile Arg Val att cgg gtc Ser Ala Glu 65 gat gat ctc Asp Asp Lev 80 tct aat att	Met  gga att caa gca att  Gly Ile Gln Ala Ile  -30  aat tta ctt ttt gac  Asn Leu Leu Phe Asp  -10  cca ccc atc att ctt  Pro Pro Ile Ile Leu  5  tca gtg ttg tct gcc  Ser Val Leu Ser Ala  20  aag ata gaa aaa gta  Lys Ile Glu Lys Val  35  ctta caa aat atg gaa  Leu Gln Asn Met Glu  55  tct aac aca gag gaa  1 Ser Asn Thr Glu Glu  70  cac ttg aaa atc tta  1 His Leu Lys Ile Leu  85  ttt cag gca tta aca	116 164 212 260 308 356 404

WO 99/31236 -65- PCT/IB98/02122

90 95	200
90 95 aag gag acg gtg gct cag gga gta aag gaa ggo	100 cag ttg agc aaa cag 596
Lys Glu Thr Val'Ala Gln Gly Val Lys Glu Gly	Gln Leu Ser Lys Gln
105 110	115
aag tgt tcc tct gca ttt caa aac ctt ctt cct Lys Cys Ser Ser Ala Phe Gln Asn Leu Leu Pro	
120 125 130	•
gtg gaa gat ttt att aaa atc cta cgt gaa gtt	
Val Glu Asp Phe Ile Lys Ile Leu Arg Glu Val	Asp Lys Ala Leu Ala
140 145 gat gac ttg gaa aaa aac ttc cca agt ttg aag	150 gtt cag act 734
Asp Asp Leu Glu Lys Asn Phe Pro Ser Leu Lys	
155 160	165
taaaacctga attggaatta cttctgtaca agaaataaac	<del>-</del>
aaaaaaaaa	. 804
<210> 89	
<211> 802 <212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	•
<222> 199801	
<221> polyA_signal	•
<222> 780785	
	·
<221> polyA_site	
<222> 791802	
<222> 791802  <400> 89  agtcaccgcc tgcttcgcac tgagcctccc gactcagact	ctgagtccag ctccgaagag 60
<222> 791802  <400> 89  agtcaccgcc tgcttcgcac tgagcctccc gactcagactgaagaggaat tcggtgtggt tggaaatcgc tctcgctttg	ccaagggaga ctatttacga 120
<222> 791802  <400> 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagactgaagaggaat tcggtgtggt tggaaatcgc tctcgctttgtgctgctaga tctgtcatcc	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180
<222> 791802  <400> 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagactgaagaggaat tcggtgtggt tggaaatcgc tctcgctttgtgctgcaaga tctgttatcc gctctgtggt tttgtcatcctgtgtttggct tggtgtggt atg cag gtt gct ctc aag	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcd tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 cagc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 gaac aaa gtc tgg ata 375
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcd tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 g aac aaa gtc tgg ata 375 Asn Lys Val Trp Ile
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcd tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 g aac aaa gtc tgg ata 375 Asn Lys Val Trp Ile 55
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcd tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 g aac aaa gtc tgg ata 375 Asn Lys Val Trp Ile 55 gttg act tct gca gtg 423
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 g aac aaa gtc tgg ata 375 Asn Lys Val Trp Ile 55 ttg act tct gca gtg 423 Leu Thr Ser Ala Val 75
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 g aac aaa gtc tgg ata 375 Asn Lys Val Trp Ile 55 ttg act tct gca gtg 423 Leu Thr Ser Ala Val 75 gac ttg att agc ctg 471
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtggt tggaaatcgc tctcgcttc tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 cagc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 g aac aaa gtc tgg ata 375 Asn Lys Val Trp Ile 55 ttg act tct gca gtg 423 Leu Thr Ser Ala Val 75 gac ttg att agc ctg 471 Asp Leu Ile Ser Leu
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgcttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 g aac aaa gtc tgg ata 375 Asn Lys Val Trp Ile 55 ttg act tct gca gtg 423 Leu Thr Ser Ala Val 75 a gac ttg att agc ctg 471 Asp Leu Ile Ser Leu 90
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtggt tggaaatcgc tctcgcttc tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 g aac aaa gtc tgg ata 375 Asn Lys Val Trp Ile 55 ttg act tct gca gtg 423 Leu Thr Ser Ala Val 75 a gac ttg att agc ctg 471 Asp Leu Ile Ser Leu 90 a gct tcc att ggc aat 519
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 cagc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 gaac aaa gtc tgg ata 375 t Asn Lys Val Trp Ile 55 ttg act tct gca gtg 423 Leu Thr Ser Ala Val 75 gac ttg att agc ctg 471 Asp Leu Ile Ser Leu 90 gct tcc att ggc aat 519 Ala Ser Ile Gly Asn 105
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 cagc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 g aac aaa gtc tgg ata 375 t Asn Lys Val Trp Ile 55 g ttg act tct gca gtg 423 Leu Thr Ser Ala Val 75 gac ttg att agc ctg 471 Asp Leu Ile Ser Leu 90 g gct tcc att ggc aat 519 Ala Ser Ile Gly Asn 105 cta cag aaa act gtg 567
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgcttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 gaac aaa gtc tgg ata 375 Asn Lys Val Trp Ile 55 ttg act tct gca gtg 423 Leu Thr Ser Ala Val 75 a gac ttg att agc ctg 471 Asp Leu Ile Ser Leu 90 gct tcc att ggc aat 519 Ala Ser Ile Gly Asn 105 a cta cag aaa act gtg 567 a Leu Gln Lys Thr Val
<pre>&lt;222&gt; 791802  &lt;400&gt; 89 agtcaccgcc tgcttcgcac tgagcctccc gactcagact gaagaggaat tcggtgtggt tggaaatcgc tctcgctttg tgctgcaaga tctgttatcc gctctgtggt tttgtcatcc tgtgttggct tggtgtgg atg cag gtt gct ctc aag</pre>	ccaagggaga ctatttacga 120 ttgctgcctg tgttgtggcc 180 gag gat ctg gat gcc 231 Glu Asp Leu Asp Ala 10 cag aaa agc tca ttc 279 Gln Lys Ser Ser Phe 25 agc aag caa aaa caa 327 Ser Lys Gln Lys Gln 40 aac aaa gtc tgg ata 375 Asn Lys Val Trp Ile 55 ttg act tct gca gtg 423 Leu Thr Ser Ala Val 75 agac ttg att agc ctg 471 Asp Leu Ile Ser Leu 90 agct tcc att ggc aat 519 Ala Ser Ile Gly Asn 105 cta cag aaa act gtg 567 Leu Gln Lys Thr Val 120

Met Pro His Ser Ser Leu  -35  cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  10  15  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  Met Pro His Ser Ser Leu  -35  10  103  15  15  16  17  18  19  247					٠												
His Phe Leu Lys Glu Thr Pro Gly Ser Asn Oln Ile Ile Pro Ser Pro 140 145 150 150 155 155 166 155 170 168 202 202 202 202 202 202 202 202 202 20	_		His	Lys'	Lys			Glu	Leu	Leu	Gln		Asp	Met	Asn	Gln	
140	cac	ttc	ttg	aag	gag	act	cct	gga	agc	aac	cag	atc	att	ccg	tca	cct	663
tea gec aca tea gaa ett gac aat aaa acc cac agt gag aat ttg aaa Ser Ala Thr Ser Glu Leu Asp Asn Lys Thr His Ser Glu Asn Leu Lys 160 165 170 cag atg ggt gat aga tet gec act etg aaa aga cag tet ttg gac cac Gln Met Gly Asp Arg Ser Ala Thr Leu Lys Arg Gln Ser Leu Asp Gln 175 180 gtc acc acc aga aca gat aca gtc aaa atc caa aaa aaa aa a 802 Val Thr Asn Arg Thr Asp Thr Val Lys Ile Gln Lys Lys Lys 190 2210> 90 2211> 1490 2212> DNA 2213> Homo sapiens 2220> 2212> CDS 2222> 381174 2221> sig_peptide 2222> 381174 2221> polyA_signal 2222> 14521457 2221> polyA_signal 2222> 14521457 2221> polyA_signal 2222> 14781490 2400> 90 teatcatcac gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg Met Pro His Ser Ser Leu -15 cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc aga ag gag ttg tet ctg agt gcc tgc tgc gtg acc ctt tgg ggg cta gga gag tuy Val Leu Leu Ser Ala Cys Leu Val Thr Leu Try Gly Leu Gly Glu -15 -10 -26 -27 -27 -28 -27 -28 -27 -28 -28 -29 -29 -29 -29 -29 -20 -20 -20 -20 -20 -20 -20 -20 -20 -20	His :	Phe	Leu	Lys			Pro	Gly	Ser	Asn		Ile	Ile	Pro	Ser		
Ser Ala Thr Ser Glu Leu Asp Asn Lys Thr His Ser Glu Asn Leu Lys 160																	211
160 165 170 170 180 180 181 181 181 181 181 181 181 18	tca	gcc	aca	tca	gaa	ctt	gac	aat	aaa	acc	cac	agt	gag	aat	ttg	aaa	/11
cag atg ggt gat aga tct gcc act ctg aaa aga cag tct ttg gac caa         759           Gln Met Gly Asp Arg Ser Ala Thr Leu Lys Arg Gln Ser Leu Asp Gln         185           gtc acc aca cag ac ac gat aca gta aca gta aaa atc caa aaa aaa aaa aa         802           Val Thr Asn Arg Thr Asp Thr Val Lys Ile Gln Lys Lys Lys         190           190         195         200           <210> 90         2212> DNA           <2112> INA         2213> Homo sapiens           <222> 381174         2223 381174           <221> Sig_peptide         2222> 38148           <222> 38148         2223> Non Heijne matrix           sccre 7.3         sec T.3           seq LLSACLVTLWGLG/EP           <221> polyA_signal           <222> ltf21457           <221> polyA_side           <222> ltf81490           <400> 90           tcat cat ca tc cat cag tgtcccggag gcagaag atg ccc cac tcc agc ctg           cat ca tca tcc atc cgt tccc agg ggt cac ggg gcc cag aag gca gc           cat ca tca tcc atc cgt tccc agg ggt cac ggg gcc cag aag gca gc           cat cca tca tcc atc cgt tccc agg ggt cac ggg gcc cag aag gca gc           tis Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala           -30         -25           tcg gtt ct ct ctg agt gcc ttg ctg ctg ctg ctg tgg ggg ctg ggg           L	ser .	Ala	Thr			Leu	Asp .	ASN	гуѕ		HIS	ser	GIU	ABII		Буs	
Clin Met Gly Amp arg Ser Ala Thr Lew Lys Arg Gln Ser Lew Amp Gln 175   180   185   185   185   185   185   185   185   185   180   185   185   180   185   180   185   180   185   180   185   190   195   195   200	cad	ata	aat			tct	acc	act	cta		aga	cag	tct	tta		caa	759
gtc acc aac agg aca gat aca gta aaa atc caa aaa aaa aaa aa ac val Thr Asn Arg Thr Asp Thr Val Lys Ile Gln Lys Lys Lys 190 195 200 200 200 200 200 200 200 200 200 20	Gln	Met	Glv	Aso	Ara	Ser	Ala	Thr	Leu.	Lys	Arq	Gln	Ser	Leu	Asp	Gln	
Val Thr Asn Arg Thr Asp Thr Val Lys Ile Gin Lys Lys Lys  190  2210										• .	_				_		
<pre></pre>															a		802
<pre> &lt;210&gt; 90 &lt;211&gt; 1490 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;2221 Sig_peptide &lt;222&gt; 38148 &lt;222&gt; 38148 &lt;222&gt; Von Heijne matrix</pre>	Val	Thr	Asn	Arg	Thr	Asp	Thr	Val	Lys	Ile	Gln	Lys		Lys			•
<pre>&lt;211&gt; 1490 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 381174  </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 38148 </pre> <pre> &lt;223&gt; Von Heijne matrix</pre>			190			٠.		195					200				,
<pre>&lt;211&gt; 1490 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 381174  </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 38148 </pre> <pre> &lt;223&gt; Von Heijne matrix</pre>																	•
<pre>&lt;211&gt; 1490 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 381174  </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 38148 </pre> <pre> &lt;223&gt; Von Heijne matrix</pre>																	
<pre>&lt;211&gt; 1490 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 381174  </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 38148 </pre> <pre> &lt;223&gt; Von Heijne matrix</pre>	-210	<b>&gt;</b> 90															
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  </pre> <pre>&lt;220&gt; &lt;221</pre>																	
<pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 381174  &lt;221&gt; sig_peptide &lt;222&gt; 38148 &lt;223&gt; Won Heijne matrix</pre>									•	•	٠						
<pre>&lt;221&gt; CDS &lt;222&gt; 381174  &lt;221&gt; sig_peptide &lt;222&gt; 38148 &lt;223&gt; Von Heijne matrix</pre>	<213	> . Ho	mo s	apie	ns												
<pre>&lt;221&gt; CDS &lt;222&gt; 381174  &lt;221&gt; sig_peptide &lt;222&gt; 38148 &lt;223&gt; Von Heijne matrix</pre>																	
<pre>&lt;222&gt; 381174  &lt;221&gt; sig_peptide &lt;222&gt; 38148 &lt;223&gt; Von Heijne matrix</pre>			_														•
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 38148 &lt;223&gt; Von Heijne matrix</pre>																	
<pre>&lt;222&gt; 38148 </pre> <pre>&lt;223&gt; Von Heijne matrix</pre>	<222	> 38	11	. 74													
<pre>&lt;222&gt; 38148 </pre> <pre>&lt;223&gt; Von Heijne matrix</pre>	<221	> si	a pe	entid	le							•					*
score 7.3 seq LLSACLVTLWGLG/EP  <221> polyA_signal <222> 14521457  <221> polyA_site <222> 14781490  <400> 90 tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg Met Pro His Ser Ser Leu -35  cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -20 ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag teu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu -15 -10 -5 1 cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu 5 10 15 cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gag gag ctg Gln Leu Gly Leu Leu La Asn Gly Val Cys Ser Leu Ala Glu Glu Leu 20 cgc cac act cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg 35 40 gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c																	
<pre>seq LLSACLVTLWGLG/EP  &lt;221&gt; polyA_signal &lt;222&gt; 14521457  &lt;221&gt; polyA_site &lt;222&gt; 14781490  &lt;400&gt; 90 tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg</pre>					mat	rix								•			
<pre>&lt;221&gt; polyA_signal &lt;222&gt; 14521457  &lt;221&gt; polyA_site &lt;222&gt; 14781490  &lt;400&gt; 90 tcatcatcac gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg</pre>																	•
<pre>&lt;222&gt; 14521457  &lt;221&gt; polyA_site &lt;222&gt; 14781490  &lt;400&gt; 90 tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg</pre>		s€	q LI	LSACI	'ALL'	NGLG/	/EP										
<pre>&lt;222&gt; 14521457  &lt;221&gt; polyA_site &lt;222&gt; 14781490  &lt;400&gt; 90 tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg</pre>							•										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 1478. 1490  &lt;400&gt; 90 tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg</pre>		_	_	_													
<pre>&lt;222&gt; 14781490  &lt;400&gt; 90 tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg</pre>	<222	.> 14	134.	. 143													
<pre>&lt;222&gt; 14781490  &lt;400&gt; 90 tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg</pre>	<221	og <.	olvA	site	2												
tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg  Met Pro His Ser Ser Leu  -35  Cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  Ctt gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  10  15  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c		_		_													
tcatcatcca gagcagccag tgtccgggag gcagaag atg ccc cac tcc agc ctg  Met Pro His Ser Ser Leu  -35  Cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  Ctt gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  10  15  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c																	i
Cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc ttg ctg gtg acc ctt ttgg ggg cta gga gag Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  10  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg gg agg act gtg cgg Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	<400	)> 9(	)			•											
Cat cca tcc atc ccg tgt ccc agg ggt cac ggg gcc cag aag gca gcc  His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala  -30  -25  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  10  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	tcat	cat	cca g	gagca	agcc	ag t	gtcc	ggga	g gc	agaa	g at	g cc	c ca	c to	c ag	gc ctg	55
cat cca tcc atc cag tgt ccc agg ggt cac ggg gcc cag aag gca gcc       103         His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -20       -20         ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag       151         Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu -15 -10 -5 1       -10 -5 1         cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg 199       Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu 5 10 15         cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg 15       15         cag ctg gga ctg ctg tta acc ggg gtc tgc agc ctg gct gag gag ctg 247       247         Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu 20 25 30       295         cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg 295       295         Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg 35 40 45       45         gcc tgc ctg ggc tgc ccc ctc cgc cgc cgt ggg gcc ctg ttg ctg c											ME	L PI			1 30	. Deu	
His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala -30 -25 -25 -20  ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu -15 -10 -5 1 cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu 5 10 15 cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu 20 25 30 cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg 35 40 45 gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	cat	cca	tcc	atc	cca	tat	ccc	agg	aat	cac	aaa	acc			a aca	a gcc	103
ttg gtt ctg ctg agt gcc tgc ctg gtg acc ctt tgg ggg cta gga gag  Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15	His	Pro	Ser	Ile	Pro	Cys	Pro	Arg	Gly	His	Gly	Ala	Glr	Lys	. Ala	a Ala	
Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu  -15  -10  -5  1  cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5  10  15  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  45  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c						•		_	-		-				٠		
-15																	151
cca cca gag cac act ctc cgg tac ctg gtc ctc cac cta gcc tcc ctg  Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5 10 15  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20 25 30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35 40  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	Leu	Val	Leu	Leu	Ser	Ala	Cys	Leu	Val	Thr		Trp	Gly	/ Le	ı Gl		
Pro Pro Glu His Thr Leu Arg Tyr Leu Val Leu His Leu Ala Ser Leu  5 10 15  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20 25 30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35 40 45  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c											_						
5 10 15  cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu 20 25 30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg 35 40 45  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	cca	cca	gag	cac	act	ctc	cgg	tac	ctg	gto	cto	cac	cta	gc	c tc	c ctg	199
cag ctg gga ctg ctg tta aac ggg gtc tgc agc ctg gct gag gag ctg  Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu  20  25  30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  45  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	Pro	Pro	GIu		Thr	Leu	Arg	туг		val	. Let	ı Hle	ter		a se	r beu	
Gln Leu Gly Leu Leu Leu Asn Gly Val Cys Ser Leu Ala Glu Glu Leu 20 25 30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg 295  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg 35 40 45  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	636	c+ c		_	cta	++=	220	aac		tac	. 200	· ctc	r act		a da	a cta	247
20 25 30  cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg 295  Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35 40 45  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c																	
cgc cac atc cac tcc agg tac cgg ggc agc tac tgg agg act gtg cgg Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg 35 40 45 gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	0111	200	-	200	200					. 0,1							
Arg His Ile His Ser Arg Tyr Arg Gly Ser Tyr Trp Arg Thr Val Arg  35  40  45  gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	cqc	cac		cac	tcc	agg	tac		ggg	ago	tac	t tgg		gac	t gt	g cgg	295
gcc tgc ctg ggc tgc ccc ctc cgc cgt ggg gcc ctg ttg ctg c	Arg	His	Ile	His	Ser	Arg	Tyr	Arc	Gly	/ Sei	Ty:	r Tr	Ar	Th:	r Va	l Arg	
Ala Cys Leu Gly Cys Pro Leu Arg Arg Gly Ala Leu Leu Leu Leu Ser  50 55 60 65  atc tat ttc tac tac tcc ctc cca aat gcg gtc ggc ccg ccc ttc act 391		35					40					45					
50 55 60 65 atc tat ttc tac tac tcc ctc cca aat gcg gtc ggc ccg ccc ttc act 391																	343
atc tat ttc tac tac tcc ctc cca aat gcg gtc ggc ccg ccc ttc act 391		Cys	Leu	Gly	Cys		Leu	Arç	g Arg	Gly		a Lei	ı Le	u Le	u Le		
					. <b>.</b>									~ ~~	a +-		201
THE TYL FIRE TYL TYL SEL DEG FLO WRIT WIR AND AND ALO ELO FIRE THE																	191
	TTE	IVI	rne	: Iyr	ıyı	. ser	. net	PIC	J ASI	1 WT	ı va.	T 01	y PI	) PI	U PI	- IIII	

			1	70					75					80		
tgg	atg	ctt	gcc	ctc	ctg	ggc	ctc	tcg	cag	gca	ctg	aac	atc	ctc	ctg	439
Trp	Met	Leu		Leu	Leu	Gly	Leu	Ser	Gln	Ala	Leu	Asn		Leu	Leu	
			85	- •				90					95			407
ggc	ctc	aag	ggc	ctg	gcc	cca	gct	gag	atc	COT	gca	gtg	tgt	gaa	aaa	487
GIY	Leu	ьуs	GIA	Leu	Ala	Pro	105	Glu	тте	ser	Ala	110	Cys	Gru	пÀг	
000	a a t	_	220	ata	acc	cat		ctg	aca	taa	tca		tac	atc	gga .	535
								Leu								
017	115					120	,				125	-1-	- , -		2	
tat	ctg	cgg	ctg	atc	ctg	cca	gag	ctc	cag	gcc	cgg	att	cga	act	tac	583
Tyr	Leu	Arg	Leu	Ile	Leu	Pro	Glu	Leu	Gln	Ala	Arg	Ile	Arg	Thr	Tyr	
130					135					140					145	
								cgg								631
Asn	Gln	His	Tyr		Asn	Leu	Leu	Arg	-	Ala	Val	Ser	GIn		Leu	•
			at =	150	++~	~~~	+~+	~~~	155	cct	~~+	226	cta	160	ata	679
								ggg Gly								075
171	110	שבע	165	110	DCu	,,op	Cyb	170			шр		175			
act	qac	ccc		att	cqc	ttc	ctg	gat	aaa	ctg	ccc	cag	cag	acc	ggt	727
								Asp								
	_	180					185					190				•
								gtt								775
Asp	_	Ala	Gly	Ile	Lys		Arg	Val	Tyr	Ser		Ser	Ile	Tyr	Glu	
	195					200					205					000
								ggc Gly								823
210	ьeu	GIU	ASII	GIY	215	Arg	WIG	Gly	1111	220	VAI	neu	GIU	ıyı	225	
	ccc	tta	cag	act		ttt	acc	atg	tca		tac	agt	caa	act		871
								Met								
				230					235		-			240	-	
								cag								919
Phe	Ser	Arg		Asp	Arg	Leu	Glu	Gln		Lys	Leu	Phe		Arg	Thr	
			245					250					255			0.65
								cct								967
ьeu	GIU	260	me	Leu	Ala	Asp	265	Pro	GIU	Ser	GIII	270	ASII	Cys	Arg	
ctc	att		tac	caq	gaa	cct		gat	gac	aσc	agc		tca	cta	tcc	1015
								Asp								
	275		•			280		-	-		285					
cag	gag	gtt	ctc	cgg	cac	ctg	cgg	cag	gag	gaa	aag	gaa	gag	gtt	acc	1063
	Glu	Val	Leu	Arg		Leu	Arg	Gln	Glu		Lys	Glu	Glu	Val		
290					295					300					305	
gtg	ggc	agc	ttg	aag	acc	tca	gcg	gtg	CCC	agt	acc	tcc	acg	atg	CCC	1111
val	GIY	ser	ren	195 310	inr	Ser	Ala	Val	315	Ser	Inr	ser	Ini	320	sei	
caa	gag	cct	gag		ctc	ctc	agt	gga		gga	aad	ccc	ctc		ctc	1159
															Leu	
			325					330		-	•		335			
cgc	acg	gat	ttc	tct	tga	gacc	cag	ggtc	acca	gg c	caga	gcct	c ca	gtgg	tctc	1214
Arg	Thr	Asp	Phe	Ser												
		340														
	-	_	_		_		_		_	_			_		tccttc	1274
															gtcccc	1334
															gatcat	1394 1454
		_						a aa			ayc	gryc	aaa	ayıt	tttcat	1494
uaa		220	-ycc	4909	ca c	LLAA	uuaa	<u> </u>	<b>~~</b>							7470

<212> DNA <213> Homo sapiens	٠.
<220> <221> CDS <222> 26361	
<221> polyA_site <222> 350361	٠
<pre>&lt;400&gt; 91 tcgagaagct gcccttagc caacc atg ccg tct gag ggt cgc tgc tgg gag</pre>	52
acc ttg aag gcc cta cgc agt tcc gac aaa ggt cgc ctt tgc tac tac Thr Leu Lys Ala Leu Arg Ser Ser Asp Lys Gly Arg Leu Cys Tyr Tyr 10 15 20 25	100
cgc gac tgg ctg ctg cgc cgc gag gat gtt tta gaa gaa tgt atg tct Arg Asp Trp Leu Leu Arg Arg Glu Asp Val Leu Glu Glu Cys Met Ser 30 35 40	148
Ctt ccc aag cta tct tct tat tct gga tgg gtg gta gag cac gtc cta Leu Pro Lys Leu Ser Ser Tyr Ser Gly Trp Val Val Glu His Val Leu 45 50 55	196
ccc cat atg cag gag aac caa cct ctg tct gag act tcg cca tcc tct Pro His Met Gln Glu Asn Gln Pro Leu Ser Glu Thr Ser Pro Ser Ser 60 65 70	244
acg tca gct tca gcc cta gat caa ccc tca ttt gtt ccc aaa tct cct Thr Ser Ala Ser Ala Leu Asp Gln Pro Ser Phe Val Pro Lys Ser Pro 75 80 85	292
gac gca agc tct gcc ttt tcc cca gcc tcc cct gca aca cca aat gga Asp Ala Ser Ser Ala Phe Ser Pro Ala Ser Pro Ala Thr Pro Asn Gly 90 95 100 105	340
acc aag ggc aaa aaa aaa aaa Thr Lys Gly Lys Lys Lys 110	361
<210> 92 <211> 605	
<212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 3131	
<221> polyA_site <222> 591605	
<pre>&lt;400&gt; 92 ca tcc ctt ccc cag gct tta tgg ttc cag ttc ttc tac cac tct gga    Ser Leu Pro Gln Ala Leu Trp Phe Gln Phe Phe Tyr His Ser Gly    1</pre>	47
agc tcc cta gaa tct cct gga atg ctt aat gga cct ttc cag cac cga Ser Ser Leu Glu Ser Pro Gly Met Leu Asn Gly Pro Phe Gln His Arg 20 25 30	95
aat tca aga att atg act cat cgg tca gca gaa aag tgaggatacc Asn Ser Arg Ile Met Thr His Arg Ser Ala Glu Lys 35 40	141
ttttcctaac ctacctgctt cccctgcagt ttcctcacaa tcttactctt tatattttag catatgtagc ttctcaggat gttaattctg ttctctctgt gttggtgtct gagcacccag	201 261

aaggtagagc caggggcact tataaaccag gagcattatt tgacaggcac ttaagaaaga

```
cactggctac gtaatcccag cactttggga ggctgaggcg gatggatcac atgaggtcag
                                                                   381
gagttcgaga ccagcctggc cagcatggtg aaaccctgtc tctactaaaa atacaaaaat
                                                                    441
tagctgggtg tggttgcaca cgcctgtaat cccagctacc tgggaggctg aggcaggaga
                                                                    501
atcgcttgaa cttgggaggc ggaggttgca gtgagcctag attttgccat tgcactccag
                                                                    561
                                                                    605
<210> 93
<211> 591
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 33..185
<221> sig_peptide
<222> 33..80
<223> Von Heijne matrix
      score 3.7
      seq IALTLIPSMLSRA/AG
<221> polyA_signal
 <222> 570..575
 <221> polyA_site
 <222> 586..591
 <400> 93
 caatcttctc agcttataac cgtctttccc tt atg cta agg ata gcc ctt aca
                                                                     53
                                    Met Leu Arg Ile Ala Leu Thr
                                        -15
 ctc atc cca tct atg ctg tca agg gct gct ggt tgg tgc tgg tac aag
                                                                     101
 Leu Ile Pro Ser Met Leu Ser Arg Ala Ala Gly Trp Cys Trp Tyr Lys
                 - 5
 gag ccc act cag cag ttt tct tac ctt tgc ctg ccc tgc ctt tca tgg
                                                                     149
 Glu Pro Thr Gln Gln Phe Ser Tyr Leu Cys Leu Pro Cys Leu Ser Trp
                            15
                                                                     195
 aat aag aaa ggc aac gtt ttg cag ctt cca aat ttc tgaagaaact
 Asn Lys Lys Gly Asn Val Leu Gln Leu Pro Asn Phe
 aatctcagat tggcagttaa agtcaaaatg ttgccaaata tttattcctt ttgcctaagt
                                                                     255
 ttggctaccc ggttcaattg ctttttattt ttaatgtctt gactcttcag agttcgtacc
                                                                     315
 tcaaaagaac aatgagaaca tttgctttgc tttctgctga atccctaatc tcaacaatct
                                                                     375
 atacctggac tgtccagttc tcctcctgtg ctatcttctc ttctatccaa gtagaatgta
                                                                     435
 tgccaggagc tccttccctc tagcaatttc tactaaaatg tccaagtaga atgtttcctt
                                                                     495
 ttacaatcaa attactgtat ttattaattt gctagaatcc agtaaatcat tttggtagct
                                                                     555
                                                                     591
 ctggctgtgc tatcaataaa aagatgaaag caaaaa
```

<210> 94 <211> 1150 <212> DNA <213> Homo sapiens <220> <221> CDS

<222> 184..915

WO 99/31236 -70- PCT/IB98/02122

<221> sig peptide <222> 184..237 ... <223> Von Heijne matrix score 3.5 seq LLGLELSEAEAIG/AD <221> polyA\_signal <222> 1119..1124 <221> polyA\_site <222> 1139..1150 <400> 94 cqqatttgac qatqqtqttc qqtcttgaat ggaaatgtag tcttaggcca gtcttaggtt tttgaacagg atagtaggta tccggagtcg attgagggcc agagcaggca ctggggttcg 120 180 gatectggge aaagttteec aegttgaggg tetegaggae geetagatet ettteecagg gcc atg gcg aac ccg aag ctg ctg gga ctg gag cta agc gag gcg gag 228 Met Ala Asn Pro Lys Leu Leu Gly Leu Glu Leu Ser Glu Ala Glu -15 -10 gcg atc ggt gct gat tcg gcg cga ttt gag gag ctg ctg ctg cag gcc 276 Ala Ile Gly Ala Asp Ser Ala Arg Phe Glu Glu Leu Leu Gln Ala tcg aag gag ctc cag caa gcc cag aca acc aga cca gaa tcg aca caa 324 Ser Lys Glu Leu Gln Gln Ala Gln Thr Thr Arg Pro Glu Ser Thr Gln 20 372 atc cag cct cag cct ggt ttc tgc ata aag acc aac tcc tcg gaa ggg Ile Gln Pro Gln Pro Gly Phe Cys Ile Lys Thr Asn Ser Ser Glu Gly 35 40 aag gtt tte ate aac ate tge cae tee eec tet ate eet eet eec gee 420 Lys Val Phe Ile Asn Ile Cys His Ser Pro Ser Ile Pro Pro Pro Ala - 50 55 468 gac gtg acc gag gag gag ctg ctt cag atg cta gag gag gac caa gct Asp Val Thr Glu Glu Glu Leu Leu Gln Met Leu Glu Glu Asp Gln Ala 70 ggg ttt cgc atc ccc atg agt ctg gga gag cct cat gca gaa ctg gat 516 Gly Phe Arg Ile Pro Met Ser Leu Gly Glu Pro His Ala Glu Leu Asp 80 85 gca aaa ggc cag gga tgt acc gcc tac gac gta gct gtc aac agc gac 564 Ala Lys Gly Gln Gly Cys Thr Ala Tyr Asp Val Ala Val Asn Ser Asp ttc tac egg agg atg cag aac agc gat ttc ttg egg gag etc gtg atc 612 Phe Tyr Arg Arg Met Gln Asn Ser Asp Phe Leu Arg Glu Leu Val Ile 110 115 120 acc atc gcc agg gag ggc ctt gag gac ata tac aac ttg cag ctg aat 660 Thr Ile Ala Arg Glu Gly Leu Glu Asp Ile Tyr Asn Leu Gln Leu Asn 130 135 ccg gaa tgg cgc atg atg aag aac cgg cca ttc atg ggc tcc atc tcg 708 Pro Glu Trp Arg Met Met Lys Asn Arg Pro Phe Met Gly Ser Ile Ser 145 150 cag cag aac atc cgc tcg gag cag cgt cct cgg atc cag gag ctg ggg 756 Gln Gln Asn Ile Arg Ser Glu Gln Arg Pro Arg Ile Gln Glu Leu Gly 165 gac ctg tac acg ccc gcc ccc ggg aga gct gag tca ggg cct gaa aag 804 Asp Leu Tyr Thr Pro Ala Pro Gly Arg Ala Glu Ser Gly Pro Glu Lys 180 185 852 cct cac ctg aac ctg tgg ctg gaa gcc ccc gac ctc ctc ttg gcc gaa Pro His Leu Asn Leu Trp Leu Glu Ala Pro Asp Leu Leu Ala Glu 200 195 900 gtt gac ctc ccc aaa ctg gat gga gcc ctg ggg ctg tcg ctg gag atc Val Asp Leu Pro Lys Leu Asp Gly Ala Leu Gly Leu Ser Leu Glu Ile 215 955 ggq aga acc gcc tgg tgatgggggg cccccaqcag ctgtatcatc tagacgctta

Gly Arg Thr Ala Trp 225 tatcccgccg cagatcaact ctcatgagag caaggcagcc ttccaccgga agagaaagca attaatggtg gccatgccgc ttctgccggt gccttcttga tcagggtgtc tccttgtgct tctgagatgt ggagaagagg ctgctggctt ccctaaaagt tgaaataaaa gatttttgcc 1135 1150 tttaaaaaaa aaaaa <210> 95 <211> 1513 <212> DNA <213> Homo sapiens .<220> <221> CDS <222> 58..1116 <221> sig\_peptide <222> 58..159 <223> Von Heijne matrix score 4 seg IAVLYLHLYDVFG/DP <221> polyA\_signal <222> 1486..1491 <221> polyA\_site <222> 1504..1513 <400> 95 57 ctgactcctg agttctcaca acgcttgacc aataagattc gggagcttct tcagcaa atg gag aga ggc ctg aaa tca gca gac cct cgg gat ggc acc ggt tac 105 Met Glu Arg Gly Leu Lys Ser Ala Asp Pro Arg Asp Gly Thr Gly Tyr -25 -30 act ggc tgg gca ggt att gct gtg ctt tac tta cat ctt tat gat gta 153 Thr Gly Trp Ala Gly Ile Ala Val Leu Tyr Leu His Leu Tyr Asp Val -10 -15 201 ttt ggg gac cct gcc tac cta cag tta gca cat ggc tat gta aag caa Phe Gly Asp Pro Ala Tyr Leu Gln Leu Ala His Gly Tyr Val Lys Gln 10 249 agt ctg aac tgc tta acc aag cgc tcc atc acc ttc ctt tgt ggg gat Ser Leu Asn Cys Leu Thr Lys Arg Ser Ile Thr Phe Leu Cys Gly Asp gca ggc ccc ctg gca gtg gcc gct gtg cta tat cat aag atg aac aat 297 Ala Gly Pro Leu Ala Val Ala Ala Val Leu Tyr His Lys Met Asn Asn 40 gag aag cag gca gaa gat tgc atc aca cgg cta att cac cta aat aag 345 Glu Lys Gln Ala Glu Asp Cys Ile Thr Arg Leu Ile His Leu Asn Lys 50 att gat cct cat gct cca aat gaa atg ctc tat ggg cga ata ggc tac 393 Ile Asp Pro His Ala Pro Asn Glu Met Leu Tyr Gly Arg Ile Gly Tyr 70 atc tat gct ctt ctt ttt gtc aat aag aac ttt gga gtg gaa aag act 441 Ile Tyr Ala Leu Leu Phe Val Asn Lys Asn Phe Gly Val Glu Lys Thr 85 90 489 cct caa agc cat att cag cag att tgt gaa aca att tta acc tct gga Pro Gln Ser His Ile Gln Gln Ile Cys Glu Thr Ile Leu Thr Ser Gly 100 105 gaa aac cta gct agg aag aga aac ttc acg gca aag tct cca ctg atg 537 Glu Asn Leu Ala Arg Lys Arg Asn Phe Thr Ala Lys Ser Pro Leu Met

120

				•					. •								
tat	gaa	tgg	tae	cag	gaa	tat	tat	gta	999	gct	gct	cat	ggc	ctg	gct		585
Tyr	Glu	Trp	Tyr	Gln	Glu	Tyr	Tyr	Val	Gly	Ala	Ala	His	Gly	Leu	Ala		
-		_	130					135					140				
gga	att	tat	tac	tac	ctg	atg	cag	CCC	agc	ctt	caa	gtg	agc	caa	999		633
Gly	Ile	Tyr	Tyr	Tyr	Leu	Met	Gln	Pro	Ser	Leu	Gln	Val	Ser	Gln	Gly		
•		145				• •	150					155					
aag	tta	cat	agt	ttg	gtc	aag	ccc	agt	gta	gac	tac	gtc	tgc	cag	ctg		681
Lys	Leu	His	Ser	Leu	Val	Lys	Pro	Ser	Val	qaA	Tyr	Val	Cys	Gln	Leu		
-	160		.,	**		165					170						
aaa	ttc	cct	tct	ggc	aat	tac	cct	cca	tgt	ata	ggt	gat	aat	cga	gat		729
Lys	Phe	Pro	Ser	Gly	Asn	Tyr	Pro	Pro	Cys	Ile	Gly	Asp	Asn	Arg	Asp		
175				•	180			••		185					190		
ctg	ctt	gtc	cat	tgg	tgc	cat	ggc	gcc	cct	999	gta	atc	tac	atg	ctc	.,	777
Leu	Leu	Val	His	Trp	Cys	His	Gly	Ala	Pro	Gly	Val	Ile	Tyr	Met	Leu		
				195				.,	200					205		٠,	
atc	cag	gcc	tat	aag	gta	ttc	aga	gag	gaa	aag	tat	ctc	tgt	gat	gcc		825
Ile	Gln	Ala	Tyr	Lys	Val	Phe	Arg	Glu	Glu	Lys	Tyr	Leu	Cys	Asp	Ala		
			210					215					220				
												ctg					873
Tyr	Gln	Cys	Ala	Asp	Val	Ile	Trp	Gln	Tyr	Gly	Leu	Leu	Lys	Lys	Gly		
		225					230		٠,٠			235					
												gcc					921
Tyr	_	Leu	Cys	His	Gly		Ala	Gly	Asn	Ala		Ala	Phe	Leu	Thr		
	240					245					250				.:		
															aag		969
	Tyr	Asn	Leu	Thr		Asp	Met	Lys	Tyr		Tyr	Arg	Ala	Cys			
255					260					265					270		
												tgc					1017
Phe	Ala	Glu	Trp	-	Leu	Glu	Tyr	Gly		His	Gly	Cys	Arg				
				275					280					285			3065
															ttc		1065
Asp	Thr	Pro		ser	ьeu	Pne	GIU		Met	Ala	GIY	Inr	300		Phe		
			290	-+-				295							<b>~~</b>		1113
															gaa		1113
neu	Ald	305	neu	. neu	vaı	PIU	310		ATG	Arg	FIIC	315		FIIC	Glu		
ctc	tas		ata (	acet.	ncca.	cc t			c ta	cato	2000	ttt		ata			1166
Leu	_	aayy	aca	gcac	gcca		gcaa	ctta	c cg	catg	accc		ctgt	464			1100
		cca	aget.	aaot	ac t	teca	ttar	t tr	ccaa	ggaa	aca	aaga	atc	aaac	tgtgga		1226
															atcatt		1286
															cctaaa		1346
															cttgga		1406
															ttaaaa		1466
												aaaa					1513
3-4			3		- <b>5</b> -		5	- 5-									

<210> 96
<211> 417
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 327..416

<221> polyA\_site <222> 404..417

<400> 96

tgttttgaqq tgttggcatt cttcgctgat ttggctgttc ccaatgttta cattatttaa 60 tcttgcaaaa atggttctgt gcacttggat gtgaaatgct gtccagtttt attttttta 120

568 603

<210> 97 <211> 603 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 63..398 <221> sig\_peptide <222> 63..206 <223> Von Heijne matrix score 4.9

seg PSLAAGLLFGSLA/GL <400> 97

aa atg cag gac act ggc tca gta gtg cct ttg cat tgg ttt ggc ttt 107 Met Gln Asp Thr Gly Ser Val Val Pro Leu His Trp Phe Gly Phe -45 ggc tac gca gca ctg gtt gct tct ggt ggg atc att ggc tat gta aaa 155 Gly Tyr Ala Ala Leu Val Ala Ser Gly Gly Ile Ile Gly Tyr Val Lys -25 gea ggc agc gtg ccg tcc ctg gct gca ggg ctg ctc ttt ggc agt cta 203 Ala Gly Ser Val Pro Ser Leu Ala Ala Gly Leu Leu Phe Gly Ser Leu -10 -15 gcc ggc ctg ggt gct tac cag ctg tct cag gat cca agg aac gtt tgg 251 Ala Gly Leu Gly Ala Tyr Gln Leu Ser Gln Asp Pro Arg Asn Val Trp 10 gtt ttc cta gct aca tct ggt acc ttg gct ggc att atg gga atg agg 299 Val Phe Leu Ala Thr Ser Gly Thr Leu Ala Gly Ile Met Gly Met Arg 25 ttc tac cac tct gga aaa ttc atg cct gca ggt tta att gca ggt gcc 347 Phe Tyr His Ser Gly Lys Phe Met Pro Ala Gly Leu Ile Ala Gly Ala agt ttg ctg atg gtc gcc aaa gtt gga gtt agt atg ttc aac aga ccc 395 Ser Leu Leu Met Val Ala Lys Val Gly Val Ser Met Phe Asn Arg Pro 60 55 cat tagcagaagt catgttccag cttagactga tgaagaatta aaaatctgca 448 tettecacta tetteaatat attaagagaa ataagegeag cattetegea teegacatte 508

tacctaaaaa aaaagacacc aaacttggca gagaggtgga aaatcagtca tgattacaaa

cctacagagg tggcgagtat gtaacacaag agctt

```
<211> 522
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> CDS
 <222> 2..163
 <221> polyA signal
 <222> 488..493
 <221> polyA_site
· <222> 511..522
 <400> 98
                                                                        49
 c gag att gcg ggc tat ggc gcc gaa ggt ttt tcg tca gta ctg gga tat
   Glu Ile Ala Gly Tyr Gly Ala Glu Gly Phe Ser Ser Val Leu Gly Tyr
                                        10
 ccc cga tgg cac cga ttg cca ccg caa agc cta cag cac cac cag tat
                                                                        97
 Pro Arg Trp His Arg Leu Pro Pro Gln Ser Leu Gln His His Gln Tyr
             20
                                 25
                                                                       145
 tge cag cgt cgc tgg cct gac cgc cgc tgc cta cag agt cac act caa
 Cys Gln Arg Arg Trp Pro Asp Arg Cys Leu Gln Ser His Thr Gln
                             40
 tcc tcc ggg cac ctt cct nntgaaggag tggctaaggt tggacaatac
                                                                       193
 Ser Ser Gly His Leu Pro
 acgttcactg cagctgctgt cggggccgtg tttggcctca ccacctgcat cagcgcccat
 gtccgcgaga agcccgacga ccccctgaac tacttccccg gtggctgcgc cnggaggcct
                                                                       313
 gactetggga geacgeacge acaactacgg gattggegee geegeetgeg tgtactttgg
                                                                       373
 catagoggcc tocotggtca agatgggccg gotggagggc tgggaggtgt ttgcaaaacc
                                                                       433
 caaggtgtga gccctgtgcc tgccgggacc tccagcctgc agaatgcgtc cagaaataaa
                                                                       493
                                                                       522
 ttctgtgtct gtgtgtgaaa aaaaaaaaa
 <210> 99
 <211> 956
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> CDS
 <222> 13..465
 <221> sig_peptide
 <222> 13..75
 <223> Von Heijne matrix
       score 3.9
       seq PVAVTAAVAPVLS/IN
 <400> 99
 ngagteggga aa atg get geg agt aen ten atg gne eeg gtg get gtg aeg
                                                                         51
               Met Ala Ala Ser Thr Ser Met Xaa Pro Val Ala Val Thr
 gcg gca gtg gcg cct gtc ctg tcc ata aac agc gat ttc tca gat ttg
                                                                         99
 Ala Ala Val Ala Pro Val Leu Ser Ile Asn Ser Asp Phe Ser Asp Leu
              - 5
. Cgg gaa att aaa aag caa ctg ctg ctt att gcg ggc ctt acc cgg gag
                                                                        147
 Arg Glu Ile Lys Lys Gln Leu Leu Ile Ala Gly Leu Thr Arg Glu
 cgg ggc cta cta cac agt agc aaa tgg tcg gcg gag ttg gct ttc tct
                                                                        195
```

WO 99/31236 -75- PCT/IB98/02122 -

Arg Gly Leu Leu His Ser Ser Lys Trp Ser Ala Glu Leu Ala Phe Ser

Arg Gly Leu Leu His Ser Ser Lys 1 25 30	rp ser Ala Giu Leu Ala Phe ser 35 40
ctc cct gca ttg cct cnt ggc cag c	
Leu Pro Ala Leu Pro Xaa Gly Gln L	
gag gaa gat gcc cag gat atg gat g	
Glu Glu Asp Ala Gln Asp Met Asp A	
ttt gac gtt aaa gag tat gat cgg g	-
Phe Asp Val Lys Glu Tyr Asp Arg A	
aat agc aag aaa gcc tat ttt ctg t	at atg tat tcc aga tat ctg gtg 387
Asn Ser Lys Lys Ala Tyr Phe Leu T	
agg gcc att tta aaa tgt cat tct g	cc ttt agt gaa aca tcc ata ttt 435
Arg Ala Ile Leu Lys Cys His Ser A	
aga acc aat gga aaa gtt aaa tct t	
Arg Thr Asn Gly Lys Val Lys Ser F	
gaatgaatgt actttataca tagcaataat	aaaaaaaaqa tatcataaat aaagttaaaa 545
aggatggtag agaagaaaat attcttagga	
atttattac tttaggttat ataaggttct	tcatgcctgt gaattaatat tattgtgtaa 665
gaattaagtt aaaaagcctg ggctgacttt	
agtatattta ttgtttttct ttcatggcta	ttaaaaagta tgactgtaaa ggacaatgca 785
agnaaaccaa cttaatactg tattgaataa	taagtacaat ttattatttt actttgaaac 845
attatgaatt tactttccta ctttttctta	
cattttatgt acntnncatt tcctagtaca	ggttgagtat cccttatttg a 956
•	
<210> 100	
<211> 1041	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 20703	·
<221> sig_peptide <222> 2094	
<222> 2094 <223> Von Heijne matrix	
score 3.9	
seq ATVGLLMLGVTLP/NS	
<221> polyA_signal	
<222> 10001005	
-221 - molya cito	
<221> polyA_site <222> 10231041	
<400> 100	
cagggtcctg catcctacc atg tcg atg	gct gtg gaa acc ttt ggc ttc ttc 52
	Ala Val Glu Thr Phe Gly Phe Phe
-25	-20 -15
atg gca act gtg ggg ctg ctg atg Met Ala Thr Val Gly Leu Leu Met	Leu Gly Val Thr Leu Pro Asn Ser
-10	-5 1
	acc and atc atc acc acc asc acc 148

tac tgg cga gtg tcc act gtg cac ggg aac gtc atc acc acc acc Tyr Trp Arg Val Ser Thr Val His Gly Asn Val Ile Thr Thr Asn Thr

15

5

250	++-	~~~	الأراث د	ctc	taa	+++	acc	tat	acc	a.c.c	a c	tee	cta	ggc	atc	196
														Gly		2,0
116	20	GIU	ASII	ביים	110	25		c <sub>y</sub> s	711 4		30	501	DCu	OLY.	Vu1 .	
+=0		tac	taa	gag	ttc		tcc	ato	cta	acc		tct	aaa	tat	att	244
														Tyr		
35	NO.	Cyo			40					45	200	-	<b>U</b> -1	-1-	50	
	acc	tac	caa	aca		ato	atc	acc	acc		ctc	cta	aac	ttc		292
_	_	_		_		_			_			_		Phe		
01	AI u	Cyb	5	55					60				<b></b> 3.	65		
aac	ctc	tta	cta		ata	aca	aac	cta		tac	acc	aac	att	999	aac	340
														Gly		
1			70	71-2			,	75	5	-1			80	2	2	
cta	gag	ctc	tcc	agg	aaa	acc	aaq	cta	aca	qcc	acc	qca		gcc	ccc	388
														Āla		
		85		_	•		90					95	•		•	•
cac	att	ctg	gcc	ggt	atc	tgc	999	atg	gtg	gcc	atc	tcc	tigg	tac	gcc	436
His	Ile	Leu	Ala	Gly	Ile	Cys	Gly	Met	Val	Ala	Ile	Ser	Trp	Tyr	Ala	
	100					105					110					
ttc	aac	atc	acc	cgg	gac	ttc	ttc	gac	ccc	ttg	tac	ccc	gga	acc	aag	484
Phe	Asn	Ile	Thr,	Arg	Asp	Phe	Phe	qaA	Pro	Leu	Tyr	Pro	Gly	Thr	Lys	
115					120					125					130	
														ctg		532
Tyr	Glu	Leu	Gly	Pro	Ala	Leu	Tyr	Leu	Gly	Trp	Ser	Ala	Ser	Leu	Ile	
				135					140					145	• •	
														ggc		580
Ser	Ile	Leu	-	Gly	Leu	Cys	Leu		Ser	Ala	Cys	Cys		Gly	Ser	
			150					155			_		160			
														cca		628
Asp	GIU	_	Pro	Ala	Ala	ser		Arg	Arg	Pro	ıyr		Ala	Pro	vaı	
+		165					170	~~~			~~~	175				676
														agc Ser		676
SEI	180		PIO	val	Ala.	185	Set	Asp	GIII	Giu	190	Asp	set	Ser	PHE	
aac			aac	ana	220		tac	ata	tag	cacc		aacc	cata	aa		723
		Tyr								cage		ggcc	cgcg	99		, 2 3
195	2,5		Ory.	9	200	****	- ] -									
	cact	atc	ttcc	cact		ccaa	aaaa	a qq	qqac	ctaa	cca	aaac	cca	ttcc	cctata	783
															cccgtg	843
															tctccc	903
															cggtgt	963
															ccgtta	1023
	_	aaa	_	_	_							-			•	1041

<210> 101

<211> 558

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 103..294

<221> sig\_peptide

<222> 103..243

<223> Von Heijne matrix score 5.9 seq TWLGLLSFQNLHC/FP

<400> 101

gaa ata ata tcc ttg aaa gag gaa tca cca tta gga aag gtg agt cag Glu Ile Ser Leu Lys Glu Glu Ser Pro Leu Gly Lys Val Ser Glu -00 -35 ggt cct ttg ttt aat gtg act agt ggc tca tca tca cca gtg acc tgg Gly Pro Leu Phe Asn Val Thr Ser Gly Ser Ser Ser Pro Val Thr Trp -25 -20 -20 Leu Gly Leu Leu Ser Phe Gln Aen Leu His Cys Phe Pro Asp Leu Pro -10 -5 -5 -6	gaa ata ata too ttg aaa gag gaa toa ooa tta gga aag gtg agt cag	٠
Gly Pro Leu Phe Asn Val Thr Ser Gly Ser Ser Pro Val Thr Trp -25 -20 -15  ttg ggc cta ctc tcc ttc cag aac ctg cat tgc ttc cca gac ctc ccc  Leu Gly Leu Leu Ser Phe Gln Asn Leu His Cys Phe Pro Asp Leu Pro -10 -5 1 act gag atg cct cta aga gcc aaa gga gtc aca act tgagcctagg 304  Thr Glu Met Pro Leu Arg Ala Lys Gly Val Asn Thr 10 15  gtgggctaca acaasaagstt ctaatttacc ttgcttcatc taggtccagg ccccaagtag cttgctgaag gaacttaaaa agtagctgtt atttattgta ttgtataaag ctaaasacatt tatttttgt gaatcgaaca aattccatgt agcaatcttt ttttctgttca cggtgtttgt gatagaacct taaattccgc aagcatcagt tttttgaaaa aattgggaatt gaccggatag taacaaggcaa agtt 2210 730  <2210	Glu Ile Ile Ser Leu Lys Glu Glu Ser Pro Leu Gly Lys Val Ser Gln	162
Leu Giy Leu Leu Ser Phe Gln Asn Leu His Cys Phe Pro Asp Leu Pro -10 -5 -5 -10 -5 -15 -3 -3 -5 -3 -5 -3 -3 -5 -3 -5 -3 -3 -5 -3 -3 -5 -3 -3 -5 -3 -3 -5 -3 -3 -5 -3 -3 -5 -3 -3 -3 -3 -3 -3 -3 -3 -3 -3 -3 -3 -3	Gly Pro Leu Phe Asn Val Thr Ser Gly Ser Ser Ser Pro Val Thr Trp	210
act gag atg cct cta aga gcc aaa gga gtc aac act tgagcctagg Thr Glu Met Pro Leu Arg Ala Lys Gly Val Asn Thr  10	ttg ggc cta ctc tcc ttc cag aac ctg cat tgc ttc cca gac ctc ccc Leu Gly Leu Leu Ser Phe Gln Asn Leu His Cys Phe Pro Asp Leu Pro	258
gtgggctaca acaaaagatt ctaatttacc ttgcttcatc taggtccagg ccccaagtag cttgctgaag gaacttaaaa agtagctgtt atttattgta ttgtataagc taaaaacatt tatttttgtt gaatcgaaac aattccatgt agcaatcttt tttctgttca cggtgttgt 484 gatagaacct taaattccgc aagcatcagt tttttgaaaa aatgggaatt gaccggatag taacaaggcaa agtt 544 548 548 548 548 548 548 548 548 548	act gag atg cct cta aga gcc aaa gga gtc aac act tgagcctagg Thr Glu Met Pro Leu Arg Ala Lys Gly Val Asn Thr	304
cttgctgaag gaacttaaaa agtagctgtt atttattgta ttgtataagc taaaaacatt tatttttgtt gaatcgaaac aattccatgt agcaatcttt tttctgttca cggtgttgt 484 gatagaacct taaattccgc aagcatcagt tttttgaaaa aatgggaatt gaccggatag 544 taacaggcaa agtt 558 <pre> &lt;210 &gt; 102</pre>		364
tattitigit gaatcgaaac aattccatgt agcaatcitt titcigitca cggtgittigt 484 gaatagaacct taaaattccgc aagcatcagt tittigaaaa aatgggaatt gaccggatag 548 taacaggcaa agtt 558 <pre> &lt;210 &gt; 102</pre>	cttgctgaag gaacttaaaa agtagctgtt atttattgta ttgtataagc taaaaacatt	424
<pre>caacaggcaa agtt  <pre> &lt;210&gt; 102 &lt;211&gt; 730 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; 221&gt; CDS &lt;222&gt; 81518  </pre> <pre> &lt;221&gt; cos</pre></pre>	tatttttgtt gaatcgaaac aattccatgt agcaatcttt tttctgttca cggtgtttgt	
<pre> &lt;210&gt; 102 &lt;211&gt; 730 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 81518 </pre> <pre> &lt;221&gt; Sig_peptide &lt;222&gt; 81173 </pre> <pre> &lt;220</pre>	gatagaacct taaattccgc aagcatcagt tttttgaaaa aatgggaatt gaccggatag	
<pre>&lt;211&gt; 730 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;221&gt; Sig_peptide &lt;222&gt; 81518  </pre> <pre> &lt;222&gt; 81173 </pre> <pre> &lt;223&gt; Von Heijne matrix</pre>	taacaggcaa agtt	558
<pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 81518  </pre> <pre>&lt;221&gt; sig_peptide &lt;222&gt; 81173 </pre> <pre>&lt;223&gt; Von Heijne matrix</pre>	<211> 730 <212> DNA	
<pre>&lt;221&gt; CDS &lt;222&gt; 81518  &lt;221&gt; sig_peptide &lt;222&gt; 81173 &lt;223&gt; Von Heijne matrix</pre>	(213) Homo papage	
<pre>&lt;221&gt; CDS &lt;222&gt; 81518  &lt;221&gt; sig_peptide &lt;222&gt; 81173 &lt;223&gt; Von Heijne matrix</pre>	<220>	••
<pre>&lt;222&gt; 81518  &lt;221&gt; sig_peptide &lt;222&gt; 81173 &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;222&gt; 81173 &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;222&gt; 81173 &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;222&gt; 81173 &lt;223&gt; Von Heijne matrix</pre>	<221> sig peptide	
score 3.9 seq ILFHGVFYAGGFA/IV  <400> 102 ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg 60 attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg 113  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30 -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc 161 Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala -20 -15 -10 -5 ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg 209 Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1 5 10 gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag 257 Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu 15 20 25 gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 35 40 atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att 11e Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 55 60 cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cat ctc 401 Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser 65 70 75	<222> 81173	
seq ILFHGVFYAGGFA/IV  <400> 102  ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg 113  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg -30 -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc 161  Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala -20 -15 -10 -5  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg 209  Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg 1 -10  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag 257  Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu 15 -20 -25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc 305  Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 -35 -40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att 353  Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 -50 -50 -50  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc 401  Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser -65 -70 -75	<223> Von Heijne matrix	
ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg atttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg 113  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg -30 -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc 161  Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala -20 -15 -10 -5  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg 209  Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg 1 5 10  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag 257  Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu 15 20 25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 35 40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att 353  Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc 401  Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser 70 75	score 3.9	
ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15  20  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu  30  35  40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile  50  50  55  60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser	seq ILFHGVFYAGGFA/IV	
ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15  20  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu  30  35  40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile  50  50  55  60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser		
Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30 -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala -20 -15 -10 -5 ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1 gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu 15 gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 55 60 cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser	-400\\ 102	
tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc  Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg  Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1  gct tta tat tac aag ttg gca gtg gag cat ccc gag  Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15  gca cag gaa gct ctg ggc cct cct ctc acc atc cat caa acc cat tat ctc aag ctc  Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu  30  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att  Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile  45  50  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc  401  Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser		60
tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc  Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg	
tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc  Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg	
Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala -20 -15 -15 -10 -5 ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg 1 gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu 15 20 gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg	
9gg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg 209  Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg -30	113
ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1 5 10  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15 20 25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu  30 35 40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile  45 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser  65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25 tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc	113
Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala	113
1	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  -10  -5	113
Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15 20 25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc 305  Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu  30 35 40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att 353  Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile  45 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc 401  Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser  65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  -10  -5  qqq ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg	113
Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15 20 25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc 305  Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu  30 35 40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att 353  Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile  45 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc 401  Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser  65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30 -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20 -15 -10 -5  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg	113
gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc 305 Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 35 40 atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att 353 Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 55 60 cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser 65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  -10  -5  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1  5  10	113 161 209
Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 35 40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att 353  Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser 65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  -10  -5  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag	113 161 209
Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 35 40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att 353  Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser 65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  -10  -5  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15  20  25	113 161 209
atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att  Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile  45 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc  Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser  65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15  20  25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc	113 161 209 257
Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile  45 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc  Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser  65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15  20  25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu	113 161 209 257
45 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc 401  Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser  65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30 -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20 -15 -10 -5  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1 5 10  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15 20 25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu  30 35	113 161 209 257 305
cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc 401 Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser 65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15  20  25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu  30  35  40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att	113 161 209 257 305
Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser 65 70 75	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg  Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg  -30  -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala  -20  -15  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg  1  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu  15  20  25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu  30  35  40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile	113 161 209 257 305
65 70 75	ctegtcatge tetttgtage gtggtgette tgttgetcae aggacaactt gcetttgatg atttteaaga gagttgtget atg atg tgg caa aag tat gea gga age agg egg Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg -30 -25  tea atg cet etg gga gea agg ate ett tte eae ggt gtg tte tat gee Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala -20 -15 -10 -5  ggg gge ttt gee att gtg tat tae etc att eaa aag ttt eat tee agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg 1	113 161 209 257 305
	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg -30 -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala -20 -15 -10 -5  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg 1 5 10  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu 15 20 25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 35 40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc	113 161 209 257 305
aga ggt ggc ccc ttt cag agg tgg cac ctt gac gag gtc ttt tta gag 449	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg -30 -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala -20 -15 -10 -5  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg 1 5 10  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu 15 20 25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 35 40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 45 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser	113 161 209 257 305
	ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt gcctttgatg attttcaaga gagttgtgct atg atg tgg caa aag tat gca gga agc agg cgg Met Met Trp Gln Lys Tyr Ala Gly Ser Arg Arg -30 -25  tca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc Ser Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala -20 -15 -10 -5  ggg ggc ttt gcc att gtg tat tac ctc att caa aag ttt cat tcc agg Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg 1 5 10  gct tta tat tac aag ttg gca gtg gag cag ctg cag agc cat ccc gag Ala Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Ser His Pro Glu 15 20 25  gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 35 40  atc gac agg gaa aac ttc gtg gac att gtt gat gcc aag ttg aag att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Asp Ala Lys Leu Lys Ile 50 55 60  cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser 70	113 161 209 257 305 353 401

WO 99/31236 -78- PCT/IB98/02122 .

·	
Arg Gly Gly Pro Phe Gln Arg Trp His Leu Asp Glu Val Phe Leu Glu 80 . 85 90	•
ctc aag gat ggt cag cag att cct gtg ttc aag ctc agt ggg gaa aac Leu Lys Asp Gly Gln Gln Ile Pro Val Phe Lys Leu Ser Gly Glu Asn 95 100 105	497
ggt gat gaa gtg aaa aag gag tagagacgac ccagaagacc cagcttgctt Gly Asp Glu Val Lys Lys Glu 110 115	548
ctagtccatc cttccctcat ctctaccata tggccactgg ggtggtggcc catctcagtg acagacactc ctgcaaccca gttttccagc caccagtggg atgatggtat gtgccagcac atggtaattt tggtgtaatt ctaacttggg cacaacgaat gctatttgtc atttttaaac tg	608 668 728 730
<210> 103	
<211> 1098	
<212> DNA <213> Homo sapiens	•
<220> <221> CDS	
<222> 66326	
<221> polyA_signal	
<222> 10661071	•
<221> polyA_site	
<222> 10871098 '	
<400> 103	
(100) 103	
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser	60 110
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc	=
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser  1 5 10 15  ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His	110
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc    Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser    1	110
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser  1 5 10 15  ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His	110
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc     Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser     1	110
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc     Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser     1	110 158 206
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc     Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser     1	110 158 206
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc  Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser  1 5 10 15  ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His  20 25 30  ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro  35 40 45  gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln  50 55 60	110 158 206 254
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc  Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser  1	110 158 206 254
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc  Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser  1 5 10 15  ttg ccc cat ggt gtc ctg gga ccc aga gca aca gga tct gtc acc cac Leu Pro His Gly Val Leu Gly Pro Arg Ala Thr Gly Ser Val Thr His  20 25 30  ctc tct ctt ctc ccc cag atc aag caa cgt gcc tca gag gct ttg ccc Leu Ser Leu Leu Pro Gln Ile Lys Gln Arg Ala Ser Glu Ala Leu Pro  35 40 45  gaa ttg ctt cgt cct gtc acc ccc atc acc aat ttt gag ggc agc cag Glu Leu Leu Arg Pro Val Thr Pro Ile Thr Asn Phe Glu Gly Ser Gln  50 55 60  tct cag gac cac agt gga atc ttt ggc ctg gta aca aac ctg gaa gag Ser Gln Asp His Ser Gly Ile Phe Gly Leu Val Thr Asn Leu Glu Glu  65 70 75  ctg gag gtg gac gat tgg gag ttc tgagcctctg caaactgtgc gcattctcca	110 158 206 254 302 356 416
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc     Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser     1	110 158 206 254 302 356 416 476
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc  Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser  1	110 158 206 254 302 356 416 476 536
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc     Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser     1	110 158 206 254 302 356 416 476
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc     Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser     1	110 158 206 254 302 356 416 476 536 596 656 716
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc	110 158 206 254 302 356 416 476 536 596 656 716 776
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc	110 158 206 254 302 356 416 476 536 596 656 716
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc	110 158 206 254 302 356 416 476 536 596 656 716 776 836
ctccctttga atgagagaaa ctaacccgct tccgaagccc ctgaaagaca ctgctccttc ctctc atg gag ttg gct ccg aca gcc cgt ctg cca cca ggc cat ggt tcc     Met Glu Leu Ala Pro Thr Ala Arg Leu Pro Pro Gly His Gly Ser     1	110 158 206 254 302 356 416 476 536 596 656 716 776 836 896

tcagagacgc aaaaaaaaaa aa	1098
	•
<210> 104	
<211> 346	
<212> DNA <213> Homo sapiens	
(213) ROMO Bapters	
<220>	
<221> CDS	
<222> 170289	
<221> sig_peptide	
<222> 170250	
<pre>&lt;223&gt; Von Heijne matrix score &lt;3.6</pre>	
seq LTLLLITPSPSPL/LF	
	•
<400> 104 ccatttgagc cccaccacgg aggttatgtg gtcccaaaag gaatgatggc caagcaatta	60
attriticete etagitetta getigettet geatigatig getitacaea aciggeatit	120
agrictocatt acacaaatag acactaattt attiggaaca agcagcaaa atg aga act	178
Met Arg Thr	
tta ttt ggt gca gtc agg gct cca ttt agt tcc ctc act ctg ctt cta	226
Leu Phe Gly Ala Val Arg Ala Pro Phe Ser Ser Leu Thr Leu Leu	
-20 -15 -10	2.24
atc acc cct tct ccc agc cct ctt cta ttt gat aga ggt ctg tcc ctc	274
Ile Thr Pro Ser Pro Ser Pro Leu Leu Phe Asp Arg Gly Leu Ser Leu -5 1 5	
aga toa goa atg tot tagoccotot cototottoo attoottoot gttggtacto	329
Arg Ser Ala Met Ser	
10 atttcttcta actttta	346
<210> 105	•
<211> 685	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 36497	
<221> polyA_signal	
<222> 650655	
<pre>&lt;221&gt; polyA_site 222. 663 685</pre>	
<222> 663685	
<400> 105	E 3
aagttctgcg ctggtcggcg gagtagcaag tggcc atg ggg agc ctc agc ggt Met Gly Ser Leu Ser Gly	53
met Gly Ser Led Ser Gly  1 5	
ctg cgc ctg gca gca gga agc tgt ttt agg tta tgt gaa aga gat gtt	101
Leu Arg Leu Ala Ala Gly Ser Cys Phe Arg Leu Cys Glu Arg Asp Val	
10 15 20 tec tea tet eta agg ett acc aga age tet gat ttg aag aga ata aat	149
Ser Ser Ser Leu Arg Leu Thr Arg Ser Ser Asp Leu Lys Arg Ile Asn	
201 001 001 202 1 2	

30

25 <sup>t</sup>,

25 6 30 35	
gga ttt tgc aca aaa cca cag gaa agt ccc gga gct cca tcc cgc act Gly Phe Cys Thr Lys Pro Gln Glu Ser Pro Gly Ala Pro Ser Arg Thr	197
40 45 50	
tac aac aga gtg cct tta cac aaa cct acg gat tgg cag aaa aag atc	245
Tyr Asn Arg Val Pro Leu His Lys Pro Thr Asp Trp Gln Lys Lys Ile	
55 60 65 70 ctc ata tgg tca ggt cgc ttc aaa aag gaa gat gaa atc cca gag act	293
Leu Ile Trp Ser Gly Arg Phe Lys Lys Glu Asp Glu Ile Pro Glu Thr	255
75 80 85	
gtc tcg ttg gag atg ctt gat gct gca aag aac aag atg cga gtg aag	341
Val Ser Leu Glu Met Leu Asp Ala Ala Lys Asn Lys Met Arg Val Lys	
90 95 100	
age age tat cta atg att gee etg aeg gtg gta gga tge ate tte atg	389
Ser Ser Tyr Leu Met Ile Ala Leu Thr Val Val Gly Cys Ile Phe Met	
105 110 115 115 acc acc acc acc acc acc acc acc acc ac	437
gtt att gag ggc aag aag gct gcc caa aga cac gag act tta aca agc Val Ile Glu Gly Lys Lys Ala Ala Gln Arg His Glu Thr Leu Thr Ser	437
120 125 130	•
ttg aac tta gaa, aag aaa gct cgt ctg aaa gag gaa gca gct atg aag	485
Leu Asn Leu Glu Lys Lys Ala Arg Leu Lys Glu Glu Ala Ala Met Lys	
135 140 145 150	
gcc aaa aca gag tagcagaggt atccgtgttg gctggatttt gaaaatccag	537
Ala Lys Thr Glu	
gaattatgtt ataacgtgcc tgtattaaaa aggatgtggt atgaggatcc atttcata	
gtatgatttg cccaaacctg taccatttcc gtatttctgc cgtagaagta gaaataaa	
ttcttaaaaa aaaaaaaaa aaaaaaaa	685
<210> 106	
<211> 554	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 18320	•
001	
<221> polyA_signal <222> 539544	
<2223 535544	
<221> polyA_site	
<222> 542554	
<400> 106	
aaccgtcgtg gggaagg atg gtg tgc gaa aaa tgt gaa aag aaa ctt ggt	50
Met Val Cys Glu Lys Cys Glu Lys Lys Leu Gly	
1 5 10	
act gtt atc act cca gat aca tgg aaa gat ggt gct agg aat acc aca	
Thr Val Ile Thr Pro Asp Thr Trp Lys Asp Gly Ala Arg Asn Thr Thr	
15 20 25	146
gaa agt ggt gga aga aag ctg aat aaa aat aaa gct ttg act tca aaa	
Glu Ser Gly Gly Arg Lys Leu Asn Lys Asn Lys Ala Leu Thr Ser Lys 30 35 40	
aaa gca aga ttt gat cca tat gga aag aat aag ttc tcc act tgt aga	
Lys Ala Arg Phe Asp Pro Tyr Gly Lys Asn Lys Phe Ser Thr Cys Arg	194
45 50 55	
	Г
att tgt aaa agt tct gtg cac caa cca ggt tct cat tac tgc cag ggc Ile Cys Lys Ser Ser Val His Gln Pro Gly Ser His Tyr Cys Gln Gly	: 242
att tgt aaa agt tot gtg cac caa cca ggt tot cat tac tgc cag ggo	: 242

-81-PCT/IB98/02122 WO 99/31236

•					
	' 80	1	35	90	
gat acc aaa aac Asp Thr Lys Asr 95				t gatggaattt	340
ctggctttct aaat	gatttt act		aattttc aagg	ataga tgtcaa	ctta 400
cagaataaca tgtt	ttaaga taa	ttaagtt taa	accagag aatti	gattg ttactc	attt 460
tgctctcatg ttct	aaacag caa	cagtgta act	agtcttt tgttg	gtaaat ggttat	tttc 520
cttataagaa ttt					554
	•				
200 200	• .	•	•		
<210> 107 <211> 1678			•		•
<211> 1076 <212> DNA		• .			
<213> Homo sap:	iens	•			,
<220>					•
<221> CDS <222> 711438					
<b>22227 711450</b>			•		
<221> sig_pept:	ide				•
<223> Von Heij:	ne matrix		·	•	
score 3.					
seq AAPV	AAGLGPVIS/R	RP.			
<221> polyA_si	gnal		•		
<222> 164416	49			•	•
00112					
<221> polyA_si	ce				
-222× 1665 16	7.8				
<222> 166516	7'8				
<400> 107					roset 60
<400> 107	gagcgct gtg	gcacgtgg aga	agagogg ggao	teggeg accets	gecet 60
<400> 107 ccgacttcca gag cccgaccctc atg	gagcgct gtg ttc gaa ga	ag cct gag t	gg gcc gag g	icg gcc cca gt	a 109
<400> 107 ccgacttcca gag cccgaccctc atg	gagcgct gtg ttc gaa ga	ag cct gag t	gg gcc gag g	cg gcc cca gt la Ala Pro Va	a 109
<400> 107 ccgacttcca gag cccgaccctc atg Met	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g	ag cct gag t lu Pro Glu 1 gta atc tca	gg gcc gag g Trp Ala Glu A -15 cga cct ccg	cg gcc cca gt la Ala Pro Va -: cct gcg gcc t	ta 109 al 10 tcc 157
<400> 107 ccgacttcca gag cccgaccctc atg Met	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N	ag cct gag t lu Pro Glu 1 gta atc tca	gg gcc gag g rp Ala Glu A -15 cga cct ccg Arg Pro Pro	geg gee eea gt la Ala Pro Va -: -: cet geg gee t Pro Ala Ala	ta 109 al 10 tcc 157
<400> 107 ccgacttcca gag cccgaccctc atg Met gcc gcg ggc ct Ala Ala Gly Le	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N	ag cct gag t lu Pro Glu 1 gta atc tca Val Ile Ser	gg gcc gag g rp Ala Glu A -15 cga cct ccg Arg Pro Pro 1	geg gee eea gt la Ala Pro Va -: cet geg gee t Pro Ala Ala !	ta 109 al 10 tcc 157 Ser
<400> 107 ccgacttcca gag cccgaccctc atg Met gcc gcg ggc ct Ala Ala Gly Le tcg caa aac aa	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro V -5 g ggc tcc a	ag cct gag t lu Pro Glu 1 gta atc tca Val Ile Ser aag cgc cgc	gg gcc gag g rp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg	geg gee eea gt la Ala Pro Va -: cet geg gee t Pro Ala Ala : 5 gee aca tta	ta 109 al 100 tcc 157 Ser
<400> 107 ccgacttcca gag cccgaccctc atg Met gcc gcg ggc ct Ala Ala Gly Le	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro V -5 g ggc tcc a	ag cct gag t lu Pro Glu 1 gta atc tca Val Ile Ser aag cgc cgc	gg gcc gag g rp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg	geg gee eea gt la Ala Pro Va -: cet geg gee t Pro Ala Ala : 5 gee aca tta	ta 109 al 100 tcc 157 Ser
<pre>&lt;400&gt; 107 ccgacttcca gag cccgaccctc atg</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I	ag cct gag t lu Pro Glu I gta atc tca Val Ile Ser aag cgc cgc Lys Arg Arg 15 ctt tcc cag	gg gcc gag g Trp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu	geg gec eca gi la Ala Pro Va -: cet geg gec i Pro Ala Ala i 5 gec aca tta i Ala Thr Leu i 20 age eta tgt i	ta 109 al 100 tcc 157 Ser cgg 205 Arg
<pre>&lt;400&gt; 107 ccgacttcca gag cccgaccctc atg</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I	ag cct gag t lu Pro Glu I gta atc tca Val Ile Ser aag cgc cgc Lys Arg Arg 15 ctt tcc cag	gg gcc gag g Trp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu	geg gec eca gi la Ala Pro Va -: cet geg gec i Pro Ala Ala i 5 gec aca tta i Ala Thr Leu i 20 age eta tgt i	ta 109 al 100 tcc 157 Ser cgg 205 Arg
<pre>&lt;400&gt; 107 ccgacttcca gag cccgacctc atg Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro V -5 g ggc tcc a s Gly Ser I a gca tct c a Ala Ser I	ag cct gag to the proof of the	gg gcc gag g rp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu cat ccc ccc His Pro Pro 35	geg gec eca gi la Ala Pro Va cet geg gec Pro Ala Ala : 5 gec aca tta : Ala Thr Leu : 20 age eta tgt Ser Leu Cys	ta 109 al 100 tcc 157 Ser cgg 205 Arg ata 253 Ile
<pre>&lt;400&gt; 107 ccgacttcca gag cccgacctc atg     Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly     10 gcc cta gag gc Ala Leu Glu Al     25 agt gac tct ga</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I a gca tct c a Ala Ser I g gag gag	ag cct gag to the proof of the	gg gcc gag g rp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu cat ccc ccc His Pro Pro 35 agg aag aag	geg gec cca gt la Ala Pro Va cct geg gec Pro Ala Ala 5 gec aca tta Ala Thr Leu 2 age cta tgt Ser Leu Cys aaa tgc ccc	205 Arg ata 253 Ile aaa 301
<pre>&lt;400&gt; 107 ccgacttcca gag cccgacctc atg</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro V -5 g ggc tcc a s Gly Ser I a gca tct c a Ala Ser I g gag gag g	ag cct gag to the proof of the	gg gcc gag g rp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu cat ccc ccc His Pro Pro 35 agg aag aag Arg Lys Lys	geg gec cca gt la Ala Pro Va cct geg gec f Pro Ala Ala f gec aca tta f Ala Thr Leu f 20 age cta tgt Ser Leu Cys aaa tge ccc Lys Cys Pro	253 263 264 265 265 265 265 265 265 265 265 265 265
<pre>&lt;400&gt; 107 ccgacttcca gag cccgacctc atg     Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly     10 gcc cta gag gc Ala Leu Glu Al     25 agt gac tct ga Ser Asp Ser Gl 40</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I a gca tct c a Ala Ser I g gag gag g u Glu Glu G	ag cct gag to the proof of the	gg gcc gag g Trp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu cat ccc ccc His Pro Pro 35 agg aag aag Arg Lys Lys	geg gec cca gt la Ala Pro Va cct geg gec f Pro Ala Ala f gec aca tta Ala Thr Leu f age cta tgt Ser Leu Cys aaa tge ccc Lys Cys Pro	ta 109 al 100 tcc 157 Ser cgg 205 Arg ata 253 Ile aaa 301 Lys 55
<pre>&lt;400&gt; 107 ccgacttcca gag cccgacctc atg</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I a gca tct c a Ala Ser I g gag gag gag u Glu Glu Gl	ag cct gag to the proof of the	gg gcc gag g rp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu cat ccc ccc His Pro Pro 35 agg aag aag Arg Lys Lys 50 gaa gta ggg	geg gec cca gt la Ala Pro Va cct geg gec f Pro Ala Ala f gec aca tta Ala Thr Leu f age cta tgt Ser Leu Cys aaa tge ccc Lys Cys Pro aag aaa ggg	ta 109 al 100 tcc 157 Ser cgg 205 Arg ata 253 Ile aaa 301 Lys 55 aag 349
<pre>&lt;400&gt; 107 ccgacttcca gag cccgacctc atg     Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly     10 gcc cta gag gc Ala Leu Glu Al     25 agt gac tct ga Ser Asp Ser Gl 40 aag gca tca tt Lys Ala Ser Ph</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I a gca tct ( a Ala Ser I g gag gag g u Glu Glu ( 45 t gcc agt ( e Ala Ser I	ag cct gag to lu Pro Glu I gta atc tca Val Ile Ser aag cgc cgc Lys Arg Arg 15 ctt tcc cag Leu Ser Gln 30 gag gag gaa Glu Glu Glu gcc tct gct Ala Ser Ala	gg gcc gag g Trp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu cat ccc ccc His Pro Pro 35 agg aag aag Arg Lys Lys 50 gaa gta ggg Glu Val Gly 65	geg gec cca get la Ala Pro Va  cct geg gec c  Pro Ala Ala s  5  gec aca tta c Ala Thr Leu s  20  age cta tgt Ser Leu Cys  aaa tge cce Lys Cys Pro  aag aaa ggg Lys Lys Gly  70	ta 109 al 100 tcc 157 Ser  cgg 205 Arg ata 253 Ile aaa 301 Lys 55 aag 349 Lys
<pre>&lt;400&gt; 107 ccgacttcca gag cccgaccctc atg     Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly     10 gcc cta gag gc Ala Leu Glu Al     25 agt gac tct ga Ser Asp Ser Gl 40 aag gca tca tt Lys Ala Ser Ph aag aaa tgt ca</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I a gca tct g a Ala Ser I g gag gag g u Glu Glu Glu Glu Glu Glu Glu Glu Glu Gl	ag cct gag to lu Pro Glu I gta atc tca Val Ile Ser aag cgc cgc Lys Arg Arg 15 ctt tcc cag Leu Ser Gln 30 gag gag gaa Glu Glu Glu gcc tct gct Ala Ser Ala	gg gcc gag g Trp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu cat ccc ccc His Pro Pro 35 agg aag aag Arg Lys Lys 50 gaa gta ggg Glu Val Gly 65 tgc agt gac	geg gec cca gt la Ala Pro Va  cct geg gec f cct geg gec f Pro Ala Ala f gec aca tta f Ala Thr Leu f age cta tgt Ser Leu Cys  aaa tge cce Lys Cys Pro  aag aaa ggg Lys Lys Gly tct gag gaa	ta 109 al 100 tcc 157 Ser  cgg 205 Arg ata 253 Ile aaa 301 Lys 55 aag 349 Lys gaa 397
<pre>&lt;400&gt; 107 ccgacttcca gag cccgaccctc atg Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro V -5 g ggc tcc a s Gly Ser I a gca tct c a Ala Ser I g gag gag g u Glu Glu Gl t gcc agt g e Ala Ser I 60 a aaa cag g n Lys Gln	ag cct gag to lu Pro Glu I gta atc tca Val Ile Ser aag cgc cgc Lys Arg Arg 15 ctt tcc cag Leu Ser Gln 30 gag gag gaa Glu Glu Glu gcc tct gct Ala Ser Ala ggc cca cct Gly Pro Pro	gg gcc gag g Trp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu cat ccc ccc His Pro Pro 35 agg aag aag Arg Lys Lys 50 gaa gta ggg Glu Val Gly 65 tgc agt gac	geg gec cca giveland Ala Pro Vala Ala Pro Vala Ala Sono Ala Ala Sono Ala Thr Leu Sono Ala Thr Leu Cysono Ala	ta 109 al 100 tcc 157 Ser  cgg 205 Arg ata 253 Ile aaa 301 Lys 55 aag 349 Lys gaa 397
<pre>&lt;400&gt; 107 ccgacttcca gag cccgaccctc atg     Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly     10 gcc cta gag gc Ala Leu Glu Al     25 agt gac tct ga Ser Asp Ser Gl 40 aag gca tca tt Lys Ala Ser Ph  aag aaa tgt ca Lys Lys Cys Gl 75</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I a gca tct g a Ala Ser I g gag gag gag u Glu Glu Glu t gcc agt g e Ala Ser I a aaa cag g n Lys Gln G	ag cct gag to lu Pro Glu I gta atc tca Val Ile Ser aag cgc cgc Lys Arg Arg 15 ctt tcc cag Leu Ser Gln 30 gag gag gaa Glu Glu Glu gcc tct gct Ala Ser Ala ggc cca cct Gly Pro Pro 80	gg gcc gag g rp Ala Glu A	geg gec cca gella Ala Pro Vala Ala Pro Vala Ala Pro Vala Ala Sono Ala Ala Sono Ala Thr Leu Sono Ala Thr Leu Cysono Ala Thr Leu	al 109 al 100 al 100 al 100 acc 157 Ser  cgg 205 Arg ata 253 Ile aaa 301 Lys 55 aag 349 Lys gaa 397 Glu
<pre>&lt;400&gt; 107 ccgacttcca gag cccgaccctc atg     Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly     10 gcc cta gag gc Ala Leu Glu Al     25 agt gac tct ga Ser Asp Ser Gl 40 aag gca tca tt Lys Ala Ser Ph  aag aaa tgt ca Lys Lys Cys Gl 75 gta gaa agg aa</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I a gca tct g a Ala Ser I g gag gag gag u Glu Glu Glu t gcc agt g e Ala Ser I a aaa cag g n Lys Gln Glu g aag aaa	ag cct gag to lu Pro Glu I gta atc tca Val Ile Ser aag cgc cgc Lys Arg Arg 15 ctt tcc cag Leu Ser Gln 30 gag gag gaa Glu Glu Glu gcc tct gct Ala Ser Ala ggc cca cct Gly Pro Pro 80 tgc cac aaa	gg gcc gag g Tp Ala Glu A	geg gec cca get la Ala Pro Va  cct geg gec Pro Ala Ala  5 gec aca tta Ala Thr Leu 20 age cta tgt Ser Leu Cys aaa tge cce Lys Cys Pro  aag aaa ggg Lys Lys Gly 70 tet gag gaa Ser Glu Glu 85 gtt gge agt	al 109 al 100 al
<pre>&lt;400&gt; 107 ccgacttcca gag cccgaccctc atg     Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly     10 gcc cta gag gc Ala Leu Glu Al     25 agt gac tct ga Ser Asp Ser Gl 40 aag gca tca tt Lys Ala Ser Ph  aag aaa tgt ca Lys Lys Cys Gl 75</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I a gca tct g a Ala Ser I g gag gag gag u Glu Glu Glu t gcc agt g e Ala Ser I a aaa cag g n Lys Gln Glu g aag aaa	ag cct gag to lu Pro Glu I gta atc tca Val Ile Ser aag cgc cgc Lys Arg Arg 15 ctt tcc cag Leu Ser Gln 30 gag gag gaa Glu Glu Glu gcc tct gct Ala Ser Ala ggc cca cct Gly Pro Pro 80 tgc cac aaa	gg gcc gag g Tp Ala Glu A	geg gec cca get la Ala Pro Va  cct geg gec Pro Ala Ala  5 gec aca tta Ala Thr Leu 20 age cta tgt Ser Leu Cys aaa tge cce Lys Cys Pro  aag aaa ggg Lys Lys Gly 70 tet gag gaa Ser Glu Glu 85 gtt gge agt	al 109 al 100 al
<pre>&lt;400&gt; 107 ccgacttcca gag cccgaccctc atg     Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly     10 gcc cta gag gc Ala Leu Glu Al     25 agt gac tct ga Ser Asp Ser Gl 40 aag gca tca tt Lys Ala Ser Ph  aag aaa tgt ca Lys Lys Cys Gl     75 gta gaa agg aa Val Glu Arg Ly     90 tct gct gaa ga</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro V -5 g ggc tcc a s Gly Ser I a gca tct o a Ala Ser I g gag gag g u Glu Glu 45 t gcc agt g e Ala Ser I 60 a aaa cag g in Lys Gln ig aag aaa	ag cct gag to lu Pro Glu I gta atc tca Val Ile Ser aag cgc cgc Lys Arg Arg 15 ctt tcc cag Leu Ser Gln 30 gag gag gaa Glu Glu Glu gcc tct gct Ala Ser Ala ggc cca cct Gly Pro Pro 80 tgc cac aaa Cys His Lys 95 aga aag agg	gg gcc gag g Tp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu cat ccc ccc His Pro Pro 35 agg aag aag Arg Lys Lys 50 gaa gta ggg Glu Val Gly 65 tgc agt gac Cys Ser Asp cag gct ctt Gln Ala Leu aaa tgc cag	geg gec cca gelala Ala Pro Vala Ala Thr Leu Pro Vala Ala Pro Vala Gly Pro Vala Gly Ser Clu Glu Ala Cat gec Ala Cat gec	ta 109 al 100 tcc 157 Ser  cgg 205 Arg ata 253 Ile aaa 301 Lys 55 aag 349 Lys gaa 397 Glu gac 445 Asp cct 493
<pre>&lt;400&gt; 107 ccgacttcca gag cccgaccctc atg     Met  gcc gcg ggc ct Ala Ala Gly Le  tcg caa aac aa Ser Gln Asn Ly     10 gcc cta gag gc Ala Leu Glu Al     25 agt gac tct ga Ser Asp Ser Gl 40 aag gca tca tt Lys Ala Ser Ph  aag aaa tgt ca Lys Lys Cys Gl gta gaa agg aa Val Glu Arg Ly     90</pre>	gagcgct gtg ttc gaa ga Phe Glu Gl -20 t ggg ccc g u Gly Pro N -5 g ggc tcc a s Gly Ser I a gca tct c a Ala Ser I g gag gag g u Glu Glu 45 t gcc agt g e Ala Ser I a aaa cag g in Lys Gln g ig aag aaa s Lys Lys	ag cct gag to lu Pro Glu I gta atc tca Val Ile Ser aag cgc cgc Lys Arg Arg 15 ctt tcc cag Leu Ser Gln 30 gag gag gaa Glu Glu Glu gcc tct gct Ala Ser Ala ggc cca cct Gly Pro Pro 80 tgc cac aaa Cys His Lys 95 aga aag agg	gg gcc gag g Tp Ala Glu A -15 cga cct ccg Arg Pro Pro 1 cag ctc ttg Gln Leu Leu cat ccc ccc His Pro Pro 35 agg aag aag Arg Lys Lys 50 gaa gta ggg Glu Val Gly 65 tgc agt gac Cys Ser Asp cag gct ctt Gln Ala Leu aaa tgc cag	geg gec cca gelala Ala Pro Vala Ala Thr Leu Pro Vala Ala Pro Vala Gly Pro Vala Gly Ser Clu Glu Ala Cat gec Ala Cat gec	ta 109 al 100 tcc 157 Ser  cgg 205 Arg ata 253 Ile aaa 301 Lys 55 aag 349 Lys gaa 397 Glu gac 445 Asp cct 493

									•							
												aca Thr			Lys .	541
120					125					130					135	
												caa Gln				589
tcc	act	tee	cct		ccc	cct	cat	aca		agc	cac	aag	cag		caa	637
				Lys								Lys				
aac	cgg	caa	aag	aat	aag	aga	aga		aag	aac	aag	ttt		cca	cct	685
												Phe 180				-
												gag				733
	185					190		. •			195	Glu			•	,. i
												cgg				781
200	Ser	PIO	vai	PIO	205	inr	Asp	Ser	HIS	210	Ala	Arg	Ala	GIY.	215	
	cqa	qcc	cac	atq		caq	caa	ctq	qat		qċc	cga	ttt	cac		829
												Arg				
ctc	aat	gaa	cag	ttg	tac	tca	999	ccc	agc	agt	gct	gca	cag	cgt	ctc	877
			235		_		_	240				Ala	245	_	.*	•
												cgc				925
		250					255					Arg 260	_	•		
												cgc				973
261	265	Val	гув	гЛе	TIP	270	reu	GIII	PIO	vaı	275	Arg	116	Ala	Arg	
gat		cac	caq	caa	cct		tcc	cta	ata	ata		gac	ttc	aac	tat	1021
												Asp				
280					285					290		_			295	
												gtg				1069
,			_	300					305			Val		310		
												gac Asp				1117
			315		_			320			_		325			1165
												ttt Phe			Ser	1105
		330					335					340	-, -			
ctg	atg	gga	acc	aac	atc	agg	gac	ttc	cta	gag	gag	gca	aat	aga	gta	1213
	345	_				350	_				355			_	Val	
_	_					_			_		_	_	_	_	ttt	1261
360	ьys	PIO	GIY	GIY	ьеи 365	Leu	гÀг	vaı	Ala	370		ser	ser	Arg	Phe 375	
	gat	att	cga	acc		cta	caa	act	ata			cta	aac	ttc	aag	1309
															Lys	2505
	-		_	380			_		3 8 5		•		•	390	_	
															ttc	1357
Ile	Val	Ser	_	Asp	Leu	Thr	Asn			Phe	Phe	Leu		_	Phe	
			395					400					405			
															ggc	1405
	~ <sub>7</sub> 5	410	O1 y	-10	210	ne u	415	-	*10	-ys	. MIG	420		. 561	GIY	
ctg	cag		caq	cca	tat	ctc			cgc	ago	tga			atct	tccttg	1458
					Cys											
	425					430										
															cctggc	
Lgc	yagc	caa	yacc	rggt	ic C	rggt	ggac	c ct	gagg	acaa	agt	.gtga	caa	aacc	tctggc	1578

1638 .· 1678

teagaettge tetaetgaag gettettggt tataagatge ataaagteae tggggetage

<210> 108 <211> 494 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 25..318· <221> sig\_peptide <222> 25..75 <223> Von Heijne matrix score 7.4 seq FFLLLQFFLRIDG/VL <221> polyA\_signal <222> 452..457 <221> polyA\_site <222> 482..494 <400> 108 aggotgagtg tgaagattag agta atg cot tot ago tit the otg otg ttg 51 Met Pro Ser Ser Phe Phe Leu Leu Leu -15 cag ttt ttc ttg aga att gat ggg gtg ctt atc aga atg aat gac acg 99 Gln Phe Phe Leu Arg Ile Asp Gly Val Leu Ile Arg Met Asn Asp Thr 1 - 5 aga ctt tac cat gag gct gac aag acc tac atg tta cga gaa tat acg 147 Arg Leu Tyr His Glu Ala Asp Lys Thr Tyr Met Leu Arg Glu Tyr Thr 15 tca cga gaa agc aaa att tct agt ttg atg cat gtt cca cct tcc ctc 195 Ser Arg Glu Ser Lys Ile Ser Ser Leu Met His Val Pro Pro Ser Leu 35 30 ttc acg gaa cct aat gaa ata tcc cag tat tta cca ata aag gaa gca 243 Phe Thr Glu Pro Asn Glu Ile Ser Gln Tyr Leu Pro Ile Lys Glu Ala 50 45 gtt tgt gag aag cta ata ttt cca gaa aga att gat cct aac cca gca 291 Val Cys Glu Lys Leu Ile Phe Pro Glu Arg Ile Asp Pro Asn Pro Ala 65 gac tca caa aaa agt aca caa gtg gaa taaaatgtga tacaacatat 338 Asp Ser Gln Lys Ser Thr Gln Val Glu 80 75 actcactatg gaatctgact ggacaccttg gctatttgta aggggttatt tttattatga 398 gaattaattg ccttgtttat gtacagattt tctgtagcct taaaggaaaa aaaaataaag 458 494 atcgttacag gcaggtttca ctcaaaaaaa aaaaac <210> 109 <211> 714

<212> DNA <213> Homo sapiens <220> <221> CDS <222> 84..332

<221> sig\_peptide <222> 84..170 <223> Von Heijne matrix score 5.2 seg PCYYLGLFQRALA/SV <221> polyA\_site <222> 702..714 <400> 109 cctatctctt ctgctggctg ggctcaatgc cgcgggtgag cgttcggccg aggctgctcc 60 taccettgag tgatgtgeet tga atg acg etg ett tea tte get get tte aeg Met Thr Leu Leu Ser Phe Ala Ala Phe Thr -25 161 get get tte tee gte ete eee tgt tae tae ett ggg etg ttt eag egg Ala Ala Phe Ser Val Leu Pro Cys Tyr Tyr Leu Gly Leu Phe Gln Arg -15 -10 209 geg etc geg teg gte tte gae cea ett tge gtt tgt tea egt gtg etc Ala Leu Ala Ser Val Phe Asp Pro Leu Cys Val Cys Ser Arg Val Leu 257 ccg aca cct gta tgt acc ttg gtc gca aca caa gcc gaa aaa ata tta Pro Thr Pro Val Cys Thr Leu Val Ala Thr Gln Ala Glu Lys Ile Leu 20 gag aat ggg ccc tgt cca acc aag gag gcg gcc cag ctt gtc ggg aag 305 Glu Asn Gly Pro Cys Pro Thr Lys Glu Ala Ala Gln Leu Val Gly Lys 45 40 30 35 352 ggc agc gtt tcc gcc aga aat gct tcg tgaaaggcac ttgagggacc Gly Ser Val Ser Ala Arg Asn Ala Ser 412 ttagcagcat cctcaacagg ccttgtaggg aatgccagaa gaagcagtcc ttggccgggc 472 ggggtggctc atgcctgtgg tcccagcact ttgggaggcc ggggcgggcg gatcacctga 532 ggtcgggagg tccagaccag cctgaccgac atggagaaac cccgtctnta ctagaaatac 592 aaaactagcc gggtgtggtg gcgcatgcct gtagtcccag ctactcggga gggtgaggca 652 ggagacgttc ttgaacccgg gaggcggagt ttgtggtgag ccgagatcgc gccattgcac 712 714

<210> 110

<211> 805

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 32..718

<221> sig\_peptide

<222> 32..100

<223> Von Heijne matrix score 7.4 seq VLLLAALPPVLLP/GA

<221> polyA\_signal

<222> 770..775

<221> polyA site

<222> 793..805

<400> 110

-																
cctc	tttc	ag c	ccʻäa	gatc	g cc	ccag	cagg	g a	tg g	gc g ly A	sb r	ag a ys I 20	tc to	gg c rp L	tg eu	52
													cta	cta	cct	100
CCC	ttc	CCC	gtg	ctc	ctt	ctg	gcc	gct	ctg	Dec	Dea	yey val	ctg	1.e11	Pro	
Pro	Phe	Pro	Val	Leu	Leu		Ala	Ala	ьeu	PIO	-5	Val	Leu	200		
	-15					-10							200	+++	200	148
999	gcg	gcc	ggc	ttc	aca	cct	tcc	ctc	gat	agc	gac	בלכ	acc	Dho	The	
Gly	Ala	Ala	Gly	Phe	Thr	Pro	Ser	Leu	Asp	ser	Asp	Pne	Thr	FILE	1111	
1				5					10					15		196
ctt	ccc	gcc	ggc	cag	aag	gag	tgc	ttc	tac	cag	CCC	atg	CCC	ctg	aag	190
Leu	Pro	Ala	Gly	Gln	Lys	Glu	Cys	Phe	Tyr	Gln	Pro	Met	PIO	Leu	гåг	
			20	٠.				25					30			244
acc	tcq	ctg	gag	atc	gag	tac	caa	gtt	tta	gat	gga	gca	gga	tta	gat	244
Ala	Ser	Leu	Glu	Ile	Glu	Tyr	Gln	Val	Leu	Asp	Gly	Ala	Gly	Leu	Asp	
		35					40					45				
átt	gat	ttc	cat	ctt	gcc	tct	cca	gaa	ggc	aaa	acc	tta	gtt	ttt	gaa	292
Tle	Asp	Phe	His	Leu	Ala	Ser	Pro	Glu	Gly	Lys	Thr	Leu	Val	Phe	Glu	
	50					55					60				•	
caa	202	aaa	tca	qat	qqa	qtt	cac	act	gta	gag	act	gaa	gtt	ggt	gat	. 340
Gln	Ara	Lvs	Ser	Asp	Gly	Val	His	Thr	Val	Glu	Thr	Glu	Val	Gly	Asp	
<i>6</i>				•	70				•	75					80	
+ = 0	ata	ttc	tac	ttt	gac	aat	aca	ttc	agc	acc	att	tct	gag	aag	gtg	. 388
m	Met	Dhe	CVS	Phe	Asp	Asn	Thr	Phe	Ser	Thr	Ile	Ser	Glu	Lys	Val	
ıyı	Mec	FIIC	CyD	85					90					95		
	++-	+++	~==	++=	atc	cta	αat	aat	atq	qqa	qaa	cag	gca	caa	gaa	436
att	משנ	Dho	Glu	Ten	Tle	Len	Asp	Asn	Met	Glv	Glu	Gln	Ala	Gln	Glu	
116	Pile	Pile	100	DC G	110			105		•			110			
			100	220	222	tat	att		aac	aca	gat	ata	ttg	gat	atg	484
caa	gaa	yat	rgg T~	Tuc	Lve	Tyr	Tle	Thr	ด้าง	Thr	Asp	Ile	Leu	Asp	Met	•
GIn	GIU	ASP	ııı	ح لابد	пуз	1 7 1	120		,			125				
		115				~~~	tcc	, • atc	900	age	ato			aga	cta	532
aaa	CTS	gaa	yac	י דום	Tou	Gly	Cor	. Tle	Ser	Ser	Ile	Lvs	Ser	Arq	Leu	
гÀг			Asp	116	neu	135					140			_		
	130	)				135	, , _++	cto	ctt	aga			gaa	act	cgt	580
ago	aaa	agt	999	cac	ald Time	Cac	. 71.	Lev	1.61	Aro	Δla	Phe	Glu	Ala	Arg	
		s Ser	GIY	HIS			1 116	, ner	, ner	155					160	
145	•				150	'		- +++	· ast			· aat	tto	tac		628
gat	cga	a aac	ata	caa	gaa	ago	: aac	n Dba	. yar	NYC	. Val	. Δer	Phe	י דיני	tct Ser	
Asp	Arg	g Asr	ı Ile			Se	ASI	1 Pile	. ASI	) WIG	, va.	L		175	Ser	
				165					170			++				676
ato	g gt1	t aat	: tta	gtg	gto	ate	ggt	ggt	gu	1 000	. 31.	. 714	. Glr	. ya	tat Tvr	
Met	: Va	l Ası			. Val	. Me	c va.	ı va.	L Val. -	1 261	. Ale	3 110	190	1 • · · · ·	l Tyr	
			180					18								718
ate	g ct	g aag	g agt	cto	ttt	ga	a ga	c aag	age	y aaa	ag'	L aye	a act	-		•
Met	t Le			r Lei	ı Phe	e G1	u As	ь гу	s Ar	a ràs	5 SE	L AIG	g Thi	•		
		19	5				20					20			+====+=	778
ta	aaac	tcca	aact	tagag	gta (	gta	acat	tg a	aaaa	tgag	g ca	taaa	aatg	caa	taaactg	805
tt	acag	tcaa	gac	caaaa	aaa a	aaaa	aaa									803
	_															

<210> 111

<211> 787

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 26..481

<221> sig\_peptide <222> 26..88

<223> Von Heijne matrix

787

## score 4.4 seq AVASSFFCASLFS/AV

<221> polyA\_signal <222> 755..760 <221> polyA\_site <222> 775..787 <400> 111 gacagectgg ataaaggete acttg atg get eag ttg gga gea gtt gtg get 52 Met Ala Gln Leu Gly Ala Val Val Ala -20 gtg gct tcc agt ttc ttt tgt gca tct ctc ttc tca gct gtg cac aag 100 Val Ala Ser Ser Phe Phe Cys Ala Ser Leu Phe Ser Ala Val His Lys -10 -5 ata gaa gag gga cat att ggg gta tat tac aga ggc ggt gcc ctg ctg 148 Ile Glu Glu Gly His Ile Gly Val Tyr Tyr Arg Gly Gly Ala Leu Leu 10 15 act tog acc ago ggo cot ggt the cat etc atg etc cot the atc aca 196 Thr Ser Thr Ser Gly Pro Gly Phe His Leu Met Leu Pro Phe Ile Thr 25 30 tca tat aag tct gtg cag acc aca ctc cag aca gat gag gtg aag aat 244 Ser Tyr Lys Ser Val Gln Thr Thr Leu Gln Thr Asp Glu Val Lys Asn 40. 45 gta cct tgt ggg act agt ggt ggt gtg atg atc tac ttt gac aga att 292 Val Pro Cys Gly Thr Ser Gly Gly Val Met Ile Tyr Phe Asp Arg Ile 60 gaa gtg gtg aac ttc ctg gtc ccg aac gca gtg cat gat ata gtg aag 340 Glu Val Val Asn Phe Leu Val Pro Asn Ala Val His Asp Ile Val Lys 75 aac tat act gct gac tat gac aag gcc ctc atc ttc aac aag atc cac 388 Asn Tyr Thr Ala Asp Tyr Asp Lys Ala Leu Ile Phe Asn Lys Ile His 90 95 cac gaa ctg aac cag ttc tgc agt gtg cac acg ctt caa gag gtc tac 436 His Glu Leu Asn Gln Phe Cys Ser Val His Thr Leu Gln Glu Val Tyr att gag ctg ttt gga ctg gaa aat gat ttt tcc cag gaa tct tca 481 Ile Glu Leu Phe Gly Leu Glu Asn Asp Phe Ser Gln Glu Ser Ser 125 taaaagggac cctgagcaag aacatttttc atagcagaca ggaggactca tccacatcgc 541 cagcaatcat aattaagcaa accgcctttt gcaccattta agatttagga aatcatccaa 601 attactttta atgtttctgc agtagaaaat gaatctaaat tcattttata gggtttgtag 661 tettttatet gttttggatt caetgtgett ttaagaaaaa gttggtaaat ttgeegttga 721

tttttctttt taacctcaaa ctaatagaat tttataaaaat attaattttc tccaaaaaaa

<210> 112 <211> 569 <212> DNA

<213> Homo sapiens

<220> <221> CDS

aaaaaa

<222> 26..562

<221> sig\_peptide

<222> 26..187

<223> Von Heijne matrix score 4.1

## seq AVVAAAARTGSEA/RV

<400 agaa	acag	gt c	•				Met	Ala	Ala	ser	-50	Ala	WIG	V & 1	<b>,</b> , , ,	52
. 45	Ser	Pro	Ser	Leu	Lys -40	Thr	Asp	Thr	Ser	-35	vaı	Den	GIU		-30	100
~~3	acg Thr	gtc Val	gca Ala	gca Ala -25	atg Met	gct Ala	gcg Ala	acc Thr	ccg Pro -20	tca Ser	gca Ala	agg Arg	gct Ala	gca Ala -15	gcc Ala	148
gcg	gtg Val	gtt Val	gcg Ala	acc	gcg Ala	gcc Ala	agg Arg	acc Thr	gga	tcc Ser	gaa Glu	gcc Ala	agg Arg 1	gtc Val	tcc Ser	196
aag Lys	gcc Ala	gct Ala	-10 ttg Leu	gct Ala	acc Thr	Lys	ctg Leu	ctq	tcc Ser	ttg Leu	agc Ser 15	ggc Gly	gtg Val	ttc Phe	gcc Ala	244
gtg Val	5 cac His	aag Lys	ccc Pro	aaa Lys	Gly	10 ccc Pro	act Thr	tca Ser	gcc Ala	gag Glu 30	ctg	ctg Leu	aat Asn	cgg Arg	ttg Leu 35	. 292
20 aag Lys	gag Glu	aag Lys	ctg Leu	ctg Leu	25 gca Ala	gaa Glu	gct Ala	gga Gly	met	cct	tct Ser	cca Pro	gaa Glu	tgg Trp 50	acc	340
aag Lys	agg Arg	aaa Lys	aag Lys	40 cag Gln	act Thr	ttg Leu	aaa Lys	Ile	45 999 Gly	cat His	gga Gly	999 Gly	act Thr	cta	gac Asp	388
agc Ser	gca Ala	gcc Ala	55 cga Arg	gga Gly	gtt Val	ctg Leu	Val	60 gtt Val	gga Gly	att Ile	gga Gly	ago Ser	gga	aca Thr	aaa Lys	436
atg Met	ttg Leu	70 acc Thr	agt Ser	atg Met	ttg Leu	Ser	75 999 Gly	tco Ser	aag	agg Arg	tat Tyr 95	act	gcc Ala	att	gga Gly	484
gaa Glu	85 ctg Leu	ggg Gly	aaa Lys	gct Ala	Thr	Asp	aca Thr	cta Lev	a gat 1 Asp	Sei	acq Thi	9 999 c Gly	aag Lys	g gta val	aca Thr	532
100 gaa Glu	qaa	aaa Lys	cct Pro	tac Tyr 120	Gly	ato	aac Asr	cto Lei	ato 111e 125	€		9				569

<210> 113

<211> 893

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 4..810

<221> sig\_peptide

<222> 4..279

<223> Von Heijne matrix
 score 6.8
 seq AVMLYTWRSCSRA/IP

<221> polyA\_signal

<222> 858..863

<221> polyA\_site

<222> 881..893

المادا

<400>	- 11	3														
gcc a																48
M	1et	Ile	Thr	His	Val	Thr	Leu	Glu	Asp	Ala	Leu	Ser		Val	Asp	
			-90					-85					-80			
ctg c																96
Leu I	Leu		Glu	Leu	Pro	Leu		Asp	Gln	Gln	Pro		He	Glu	Pro	
		-75					-70	- •				-65				7.4.4
cca c																144
Pro P	-60	sei	ser	TIE	met	-55	GIII	Ald,	ASII	Phe	-50	TIII	WPII	PILE	GIU	
gac a		aat	aca	+++	atc		aac	att	gca.	agg		att	gag	cag	act	192
Asp A																
-45	5				-40		,			-35	-2-				-30	•
aca g	gtc	cac	tcc	agc	atg	aat	gag	atg	ctg	gag	gaa	gga	cat	gag	tat	240
Thr, V																••
				-25					-20					-15		
gcg g																288
Ala V	Val	Met			Thr	Trp	Arg		Cys	Ser	Arg	Ala		Pro	Gln	
			-10,					-5		* 1			1			226
gtg a																, 336
Val I	Lys 5	Çys	ASI	GIU	Gin	10	Asn	AIG	val	GIμ	15	Tyr	GIU	nys	1111	. •
		ata	cta	a a a	cca		atc	acc	220	ctc		aag	ttc	ato	tat.	384
Val (	Glu	Val	Leu	Glu	Pro	Glu	Val	Thr	Lvs	Leu	Met	Lvs	Phe	Met	Tvr	•••
20					25				-7-	30		-1-			35	
ttt	cag	cgc	aag	gcc	atc	gag	cgg	ttc	tgc	agc	gag	gtg	aag	cgg.	ctg	432
Phe (																
				40					45				ļi	50		
tgc d	cat	gcc	gag	cgc	agg	aag	gac	ttt	gtc	tct	gag	gcc	tac	ctc	ctg	480
Cys I	His	Ala		Arg	Arg	Lys	Asp		Val	Ser	Glu	Ala		Leu	Leu	
			55					60					65		226	528
acc o																320
IIII	peu	70	пуъ	Pne	TTE	WPII	75	PHE	AIG	Val	Deu	80°	Giu	Бец	Lys	
aac	ato		tac	age	atc	aaq		gac	cac	tcc	acc		aaq	agg	qca	576
Asn																
	85	•	•			90		-			95	-	-			
gca	cag	ttc	ctg	cgg	aag	atg	gca	gat	ccc	cag	tct	atc	cag	gag	tcg	624
Ala	Gln	Phe	Leu	Arg	Lys	Met	Ala	Asp	Pro	Gln	Ser	Ile	Gln	Glu		
100					105					110					115	
cag																672
Gln	Asn	Leu	Ser			Leu	Ala	Asn	125		Arg	1 TTE	rnr	130		
ata		C26	<b>C</b> 2 2	120		at a	2+0	CCS			020	, ,,,,,,	cto		gct	720
															Ala	,,,,
200			135					140	_	-7-			145			
gac	att	qtc		ato	tqt	qte	gat	tac	tac	gag	aac	aag	ato	tac	ctg	768
Asp	Ile	Val	Asn	Ile	Cys	Val	Asp	Туг	Tyr	Glu	Ası	ı Lys	Met	Tyr	Leu	
		150					155	,				160	)			
												cto				810
Thr			Glu	Lys	His			Let	ı Lya	Val		Lev	Pro	>		
	165					170					175					
	_						jctta	C C	ctctc	cacct	tc	tctt	att	aaaa	atccgt	
ttta	aaaa	aac	aaaa	aaaa	aaa a	aa										893

<sup>&</sup>lt;210> 114 <211> 1475 <212> DNA

<sup>&</sup>lt;213> Hamo sapiens

```
<220>
<221> CDS
<222> 55..459
<221> sig_peptide
<222> 55..120
<223> Von Heijne matrix
      score 7.2
      seq GLWLALVDGLVRS/SP
<221> polyA_signal
<222> 1444..1449
<221> polyA_site
<222> 1462..1475
<400> 114
cagttccgca gctacgtgtg ggacccgctg ctgatcctgt cgcagatcgt cctc atg
                                                                   57
105
Gln Thr Val Tyr Tyr Gly Ser Leu Gly Leu Trp Leu Ala Leu Val Asp
                        -15
    -20
                                                                     153
ggg cta gtg cga agc agc ccc tcg ctg gac cag atg ttc gac gcc gag
Gly Leu Val Arg Ser Ser Pro Ser Leu Asp Gln Met Phe Asp Ala Glu
                                                                     201
ate etg gge tit tee ace eet eea gge egg ete tee atg atg tee tie
Ile Leu Gly Phe Ser Thr Pro Pro Gly Arg Leu Ser Met Met Ser Phe
                                20
            15
ate tte aac gee etc ace tgt gee etg gge ttg etg tae tte ate egg
                                                                     249
Ile Phe Asn Ala Leu Thr Cys Ala Leu Gly Leu Leu Tyr Phe Ile Arg
                            35
cga gga aag cag tgt ctg gat ttc act gtc act gtc cat ttc ttt cac
                                                                     297
Arg Gly Lys Gln Cys Leu Asp Phe Thr Val Thr Val His Phe Phe His
                        50
                                                                     345
 ctc ctg ggc tgc tgg ttc tac agc tcc cgt ttc ccc tcg gcg ctg acc
Leu Leu Gly Cys Trp Phe Tyr Ser Ser Arg Phe Pro Ser Ala Leu Thr
                    65
 tgg tgg ctg gtc caa gcc gtg tgc att gca ctc atg gct gtc atc ggg
                                                                     393
 Trp Trp Leu Val Gln Ala Val Cys Ile Ala Leu Met Ala Val Ile Gly
                                    85
 gag tac ctg tgc atg cgg acg gag ctc aag gag ata ccc ctc aac tca
                                                                     441
 Glu Tyr Leu Cys Met Arg Thr Glu Leu Lys Glu Ile Pro Leu Asn Ser
                                                                     489
 gcc cct aaa tcc aat gtc tagaatcagg ccctttggac atcccgctga
 Ala Pro Lys Ser Asn Val
         110
 cacttgggcc ccttaacacc ttgggctgct cagaccctcc agatgaggtc cagcccagat
                                                                      549
 ctgagaggaa ccctggaaat gtgaagtctc tgttggtgtg ggagagatag tgagggcctg
                                                                      609
                                                                      669
 tcaaagaagg caggtagcag tcagcatgac agctgcaaga atgacctctg tctgttgaag
                                                                      729
 ccttggtatc tgagaggtca ggaaggggac ctctttgagg gtaataacat aattggaacc
                                                                      789
 atgccactct tgagccacaa tacctgtcac cagcctgttg ttttaagaga gaaaaaaaat
 caaggatatc tgattggagc aaaccacttc tttagtcatc tgtcttacct ccctgggaca
                                                                      849
 gctgttacct ttgcagtgtt gccgaatcac agcagttacc tttgcaatgt tgccgaatca
 cagcagttct gttggagaaa cgcttggttt ccggatccag agccacagaa agaaatgtag
                                                                      969
                                                                     1029
 gtgtgaagta ttaggctgct gtcagggaga ggatggcaga tggaggcatc aagcacaagg
 aaaatgcaca acctgtgccc tgttatacac acgttcatgt gcgcccaaga acctatgact
                                                                     1089
 ttettecagt teettetace aggtececat cetgetgeca geteteaaca tageaggeca
                                                                     1149
                                                                     1209
 taggacccag agaagaatcc cagtgttgct caaagtctga ccatcataaa gacactgcct
                                                                     1269
 gtcttctagg aatgaccagg cacccagctc ccactggact ccaatttttt ttcctgcctt
                                                                     1329
  atttagaatt ctttggcggg aagggtatga tgggttccca gagacaagaa gcccaacctt
                                                                     1389
  ctggcctggg ctgtgctgat agtgctgagg gagataggaa tttgctgcta agatttttct
```

```
ttggggtgga gtttcctctg tgaggggctt gcagctatcc ttcctgtgta tacaaataca
                                                                     1475
gtattttcca tgaaaaaaa aaaaaa
<210> 115
<211> 321
<212> DNA
<213> Homo sapiens
<220>
<221> CDS 👙
<222> 48..248
<221> sig_peptide
<222> 48..161
<223> Von Heijne matrix
      score 6.3
      seg LVFALVTAVCCLA/DG
<221> polyA_signal
<222> 283..288
<221> polyA_site
<222> 308..321
<400> 115
                                                                       . 56
gctgagaaga gttgagggaa agtgctgctg ctgggtctgc agacgcg atg aat aac
                                                     Met Asn Asn
gtg cag ccg aaa ata aaa cat cgc ccc ttc tgc ttc agt gtg aaa ggc
                                                                       104
Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser Val Lys Gly
 -35
                     -30
 cac gtg aag atg ctg cgg ctg gtg ttt gca ctt gtg aca gca gta tgc
                                                                       152
His Val Lys Met Leu Arg Leu Val Phe Ala Leu Val Thr Ala Val Cys
                                     -10
               -15
 tgt ctt gcc gac ggg gcc ctt att tac cgg aag ctt ctg ttc aat ccc
                                                                       200
 Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu Phe Asn Pro
 aac ggt cct tac cag aaa aag cct gtg cat gaa aaa aaa gaa gtt ttg
                                                                       248
 Asn Gly Pro Tyr Gln Lys Lys Pro Val His Glu Lys Lys Glu Val Leu
                         20
                                                                       308
 tgattttata ttacttttta gtttgatact aagtattaaa catatttctg tattcttcca
                                                                       321
 aaaaaaaaa aaa
 <210> 116
 <211> 450
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> CDS
 <222> 25..399
 <221> sig_peptide
 <222> 25..186
 <223> Von Heijne matrix
       score 3.5
```

seq SILAQVLDQSARA/RL

ctgctccagc gctgacgccg agcc atg gcg gac gag gtg ctt gag gcg ctg Met Ala Asp Glu Glu Leu Glu Ala Leu -50	51
agg aga cag agg ctg gcc gag ctg cag gcc aaa cac ggg gat cct ggt Arg Arg Gln Arg Leu Ala Glu Leu Gln Ala Lys His Gly Asp Pro Gly -45 -40 -35 -30	99
gat gcg gcc caa cag gaa gca aag cac agg gaa gca gaa atg aga aac Asp Ala Ala Gln Gln Glu Ala Lys His Arg Glu Ala Glu Met Arg Asn -25 -20 -15	147
agt atc tta gcc caa gtt ctg gat cag tcg gcc cgg gcc agg tta agt Ser Ile Leu Ala Gln Val Leu Asp Gln Ser Ala Arg Ala Arg Leu Ser -10 -5	195
aac tta gca ctt gta aag cct gaa aaa act aaa gca gta gag aat tac Asn Leu Ala Leu Val Lys Pro Glu Lys Thr Lys Ala Val Glu Asn Tyr	243
ctt ata cag atg gca aga tat gga caa cta agt gag aag gta tca gaa Leu Ile Gln Met Ala Arg Tyr Gly Gln Leu Ser Glu Lys Val Ser Glu	291
caa ggt tta ata gaa atc ctt aaa aaa gta agc caa caa aca gaa aag Gln Gly Leu Ile Glu Ile Leu Lys Lys Val Ser Gln Gln Thr Glu Lys 40 45 50	.339
aca aca aca gtg aaa ttc aac aga aga aaa gta atg gac tct gat gaa Thr Thr Thr Val Lys Phe Asn Arg Arg Lys Val Met Asp Ser Asp Glu	387
gat gac gat tat tgaactacaa gtgctcacag actagaactt aacggaacaa Asp Asp Asp Tyr	439
70 gtctaggaca g	450
<210> 117 <211> 1173 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 101137	
<221> sig_peptide <222> 1072 <223> Von Heijne matrix     score 6.5     seq LLTLLLPPPPLYT/RH	
<221> polyA_signal	
<221> polyA_site <222> 11621173	
<pre>&lt;400&gt; 117 gagctgctt atg gga cac cgc ttc ctg cgc ggc ctc tta acg ctg ctg Met Gly His Arg Phe Leu Arg Gly Leu Leu Thr Leu Leu -20 -15 -10</pre>	51
ccg ccg cca ccc ctg tat acc cgg cac cgc atg ctc ggt cca gag tcc Pro Pro Pro Pro Leu Tyr Thr Arg His Arg Met Leu Gly Pro Glu Ser	99
gtc ccg ccc cca aaa cga tcc cgc agc aaa ctc atg gca ccg ccc cga Val Pro Pro Pro Lys Arg Ser Arg Ser Lys Leu Met Ala Pro Pro Arg 10 15 20 25	147

WO 99/31236 -92- PCT/IB98/02122

									• •							
												gca Ala				195
												gag Glu				243
												gtg Val				291
	_	60	••	٠,	-		65		.,	_		70		•		339
				_			-	٠.	_		_	cat His		_		339
					_							agg Arg			_	 387
												ttc Phe				435
			Gln	ttg				Ser	gaa			agc Ser	Met	gtg		483
												gag Glu 150				 531
		aat										cct Pro				579
											Leu	aat Asn'				627
												cgt Arg				675
									Leu			tac		His		723
								Glu				gcc Ala 230	Gln			771
cag Gln	gtg Val 235	Asp	cca Pro	agt Ser	gga Gly	gag Glu 240	Ile	gtg Val	gaa Glu	ctg Leu	gcg Ala 245	aaa Lys	ggt Gly	gca Ala	tgt Cys	819
	Trp					Tyr					Gly				cca Pro 265	867
Val	Ala	Ile	Phe	Phe 270	Val	Ile	Tyr	Thr	Asp 275	Glr	Ala	Gly	Gln	Trp 280		915
Ile	Gln	Cys	Val 285	Pro	Lys	Glu	Pro	His 290	Ser	Phe	Glr	ı Ser	295	J Leu S	Pro	963
			Pro					Arg					Asp		gtc Val	1011
		Ile					Phe					r Gly			ggc Gly	1059
	/ His					Gly					L Ala				ttg Leu 345	1107
_	-	_							tco Ser		gtct	aata	aaa	cctt	cca	1157

C210   118   C211   785   C212   786   C21		350	355		.,
2212 DNA	tctcaaaaaa aaaaa	a			1173
2212 DNA					
2212 DNA	.'				
2212 DNA	-210> 118				
2212 DNA 2213 Homo sapiens  220 CDS 2221 CDS 2222 72704  2213 copy a signal 2223 You Heijne matrix 220 seq LLLSTLVIPSAA/AP  2215 polyA_signal 2222 772777  2400 118  2221 polyA_signal 2222 772777  2400 118  250					.*
2210 CDS		ens			•
<pre> &lt;221c CDS &lt;222c 72704  </pre> <pre> &lt;221c sig_peptide &lt;222c 72161 </pre> <pre> &lt;223c Von Heijne matrix</pre>	• •				
221> sig_peptide 222> 72161  223> Voon Heijne matrix score 13.2 seq LLLLSTLVIPSAA/AP  221> polyA_signal 222> 772777  2400> 118 cggaatccgg gagtccggtg acccgggctg tggtctagca taaaggcgga gcccagaaga aggggcgggg t atg gga gaa gcc tcc cca cct gcc ccc gca agg cgg cat Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His -30 -25 -20  ctg ctg gtc ctg ctg ctc ctc tct acc ctg gtg atc ccc tcc gct Leu Leu Val Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala -15 -10 gca gct cct atc cat gat gct acc gcc caa gag agc tcc ttg gtc ctc Ala Ala Pro Ile His Aep Ala Aep Ala Glu Ser Ser Leu Gly Leu 1 5 10 aca ggc ctc cag agc cta ctc caa ggc ttc agc cga ctt ttc ctg aaa Thr Gly Leu Gln Ser Leu Leu Gln Gly Phe Ser Ala Pro Heu Leu Leu Leu Leu Leu Ser Thr Leu Val Leu Leu Leu Leu Ser Thr Gly Eu Gly Leu 1 5 10 aca ggc ctc cag agc cta ctc caa ggc ttc agc cga ctt ttc ctg aaa Thr Gly Leu Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys 20 ggt aac ctg ctt cgg gga ata gac agc tta ttc tct gcc cca atg gac Gly Asn Leu Leu Arg Gly Ile Aep Ser Leu Phe Ser Ala Pro Met Asp 40 45 ttc cgg ggc ctc cct ggg aac acc acaa gag gag aac cag gag cac Phe Arg Gly Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His 50 55 60 cag ctg ggg aac aac aac cct tcc agc cac ctc cag atc gac aag gta Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Aep Lys Val 65 60 cca ggg gag ag gag gag gag gcc ctg gta ccc atc cag aag gcc acg Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr 80 85 90 gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc ttc tgg atc att Aap Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile 100 aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg gag ggc cac Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His 115 120 125 126 127 teg ctc agc gag agc cac ag gcc ct gag ggc cac Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser					
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 72161 </pre> <pre>&lt;222&gt; 72161 </pre> <pre>&lt;223&gt; Yon Heijne matrix</pre>					
<pre>&lt;222&gt; 72.161 &lt;223&gt; Von Heijne matrix</pre>	<i>₹4225 12104</i>				
<pre>&lt;222&gt; 72.161 &lt;223&gt; Von Heijne matrix</pre>	<221> sig_peptid	le .		•	.•
score 13.2 seq LLLLSTLVIPSAA/AP  <221> polyA_signal <222> 772777  <400> 118 cggaatccgg gagtccggtg acccgggctg tggtctagca taaaggcgga gcccagaaga aggggcgggg t atg gga gaa gcc tec cca cct gcc ccc gca agg cgg cat Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His -30 -25 -20  ctg ctg gtc ctg ctg ctc ctc tct acc ctg gtc acc tcc gct Leu Leu Val Leu Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala -15 -10 -5 gca gct cct atc cat gat gct gac gcc caa gag agc tcc ttg ggt ctc Ala Ala Pro Ile His Asp Ala Asp Ala Glu Glu Ser Ser Leu Gly Leu 1	<222> 72161				
<pre></pre>	<223> Von Heijne	e matrix			
<pre>&lt;221&gt; polyA_signal</pre>	score 13.2	/ ************************************			.'
<pre>&lt;222&gt; 772777  &lt;400&gt; 118 cggaatccgg gagtccggtg acccgggctg tggtctagca taaaggcgga gcccagaaga aggggcggg t atg gga gaa gcc tcc cca cct gcc ccc gca agg cgg cat</pre>	seg Lulls.	IDVIPSAR/AL			
<pre>&lt;222&gt; 772777  &lt;400&gt; 118 cggaatccgg gagtccggtg acccgggctg tggtctagca taaaggcgga gcccagaaga aggggcggg t atg gga gaa gcc tcc cca cct gcc ccc gca agg cgg cat</pre>	<221> polvA sign	nal			
cggaatccgg gagtccggtg acccgggctg tggtctagca taaaggcgg gtccaagas aggggcgggg t atg gga gaa gcc tcc cca cct gcc ccc gca agg cgg cat  Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His  -30  ctg ctg gtc ctg ctg ctc ctc tct acc ctg gtg atc ccc tcc gct Leu Leu Val Leu Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala  -15  gca gct cct atc cat gat gct gac gcc caa gag agg tcc ttg ggt ctc Ala Ala Pro Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu 1	<222> 772777				
cggaatccgg gagtccggtg acccgggctg tggtctagca taaaggcgg gtccaagas aggggcgggg t atg gga gaa gcc tcc cca cct gcc ccc gca agg cgg cat  Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His  -30  ctg ctg gtc ctg ctg ctc ctc tct acc ctg gtg atc ccc tcc gct Leu Leu Val Leu Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala  -15  gca gct cct atc cat gat gct gac gcc caa gag agg tcc ttg ggt ctc Ala Ala Pro Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu 1					
Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His  -30  -25  ctg ctg gtc ctg ctg ctg ctc ctc tct acc ctg gtg atc ccc tcc gct  Leu Leu Val Leu Leu Leu Leu Ser Thr Leu Val IIe Pro Ser Ala  -15  gca gct cct atc cat gat gct gac gcc caa gag agc tcc ttg ggt ctc  Ala Ala Pro IIe His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu  1 5  aca ggc ctc cag agc cta ctc caa ggc ttc agc cga ctt ttc ctg aaa  254  Thr Gly Leu Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys  20  25  ggt aac ctg ctt cgg ggc ata gac agc tta ttc tct gcc ccc atg gac  Gly Asn Leu Leu Arg Gly Ile Asp Ser Leu Phe Ser Ala Pro Met Asp  35  40  45  ttc cgg ggc ctc ctc ctg gg aac tac cac aaa gag gag aac cag gag cac  Phe Arg Gly Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His  50  50  cag ctg ggg aac aac acc ctc tcc agc cac ctc cag atc gac aag gta  Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val  65  60  cac agg atg gag gag aag gcc ctg gta ccc atc cag aag gcc acg  Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val  65  60  cca gg atg gag gag aag gcc ctg gta ccc atc cag aag gcc acg  Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val  65  65  60  60  60  60  61  62  63  646  65  66  67  67  67  68  69  69  69  60  60  60  60  60  60  60	<400> 118		acto toototao	ca taaaggcgga gcccagaaga	60
Met Gly Glu Ala ser Pro Pro Ara Pro Pro Pro Ara Pro Pro Pro Pro Ara Pro	cggaatccgg gagt	coggig accogg	tcc cca cct	qcc ccc gca agg cgg cat	110
Ctg ctg gtc ctg ctg ctg ctc ctc ctc acc ctg gtg atc ccc ccc ccc gct Leu Leu Val Leu Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala -15 -10 -10 -5 -5 -10 -10 -5 -5 -10 -10 -5 -5 -10 -10 -5 -10 -10 -15 -10 -10 -15 -10 -10 -15 -10 -10 -10 -15 -10 -10 -10 -10 -10 -10 -10 -10 -10 -10	aggggcgggg L at	t Glv Glu Ala	Ser Pro Pro	Ala Pro Ala Arg Arg His	
Ctg ctg gtc ctg ctg ctg ctc ctc tta ctc tta ctc gtg gtg ctc ctc tta ctc tta gtg ctc ctc leve Leu Leu Leu Leu Ser Thr Leu Val Iie Pro Ser Ala	_ 3	0	-25	-20	3.50
Leu Leu Val Leu Leu Leu Leu Leu Ser Thr Ear Ser Thr Ser Ser Thr Ser Ser Thr Ser Ser Thr Ser Ser Ser Leu Gly Leu Leu Ser Ser Leu Gly Leu Ser Ser Leu Gly Leu Ser Thr Gly Leu Gln Ser Leu Leu Gln Glu Ser Ser Leu Gly Leu Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys Ser Ser Leu Leu Leu Leu Ser Ser Leu Leu Leu Lys Ser Ser Leu Ser Ser Leu Leu Lys Ser Ser Leu Ser Ser Leu Leu Lys Ser Ser Leu Ser Ser Leu Leu Lys Ser Ser Leu Phe Leu Lys Ser	ctg ctg gtc ctg	ctg ctg ctc	ctc tct acc c	tg gtg atc ccc tcc gct	120
gca gct cct atc cat gat gct gac gcc caa gag agc tcc ttg ggt ctc Ala Ala Pro Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu  1	Leu Leu Val Leu	Leu Leu Leu	Leu Ser Thr L	eu vai ile rio bei	•
Ala Ala Pro Ile His Asp Ala Asp Ala (In 10	_1 =		-10	~5	206
1	gca gct cct atc	cat gat gct	Asn Ala Gln G	Slu Ser Ser Leu Gly Leu	
aca ggc ctc cag agc cta ctc caa ggc ttc agc cga ctt ttc ctg aaa 254  Thr Gly Leu Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys 20 20 30 30 30 30 30 30 30 30 30 30 30 30 30	•	5	1	70	
## Ser Leu Gln Ser Leu Gln Gly Phe Ser Arg Bet 73 30  ## Ser Leu Gln Gly Phe Ser Arg Bet 73 30  ## Ser Arg Bet 73 30  ## Ser Leu Common Ser Arg Bet 73 30  ## Ser Leu Common Ser Leu Common Ser Leu Common Ser Leu Common Ser Leu Phe Ser Ala Pro Met Asp 45  ## Ser Leu Phe Ser Ala Pro Met Asp 45  ## Ser Leu Phe Ser Ala Pro Met Asp 45  ## Ser Leu Phe Ser Ala Pro Met Asp 45  ## Ser Leu Phe Ser Ala Pro Met Asp 45  ## Ser Common Ser Leu Phe Ser Ala Pro Met Asp 45  ## Ser Common Ser Leu Phe Ser Ala Pro Met Asp 45  ## Ser Common Ser Leu Phe Ser Ala Pro Met Asp 45  ## Ser Common Ser Leu Phe Ser Ala Pro Met Asp 45  ## Ser Common Ser Leu Phe Ser Ala Pro Met Asp 45  ## Ser Glu Glu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His 60  ## Ser Common Ser Common Ser Common Ser Ala Pro He Asp Lys Val 60  ## Ser Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val 65  ## Common Ser Common S		and sta sts	caa ggc ttc a	age ega ett tte etg aaa	254
ggt aac ctg ctt cgg ggc ata gac agc tta ttc tct gcc ccc atg gac Gly Asn Leu Leu Arg Gly Ile Asp Ser Leu Phe Ser Ala Pro Met Asp  40  ttc cgg ggc ctc cct ggg aac tac cac aaa gag gag aac cag gag cac Phe Arg Gly Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His  50  cag ctg ggg aac aac acc ctc tcc agc cac ctc cag atc gac aag gta Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val  65  ccc agg atg gag gag aag gag gcc ctg gta ccc atc cag aag gcc acg Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr  80  85  gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc ttc tgg atc att Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile  100  aag ctg cca cgg agg agg cgc ctg cag gcc ctg gag ggc ggc cac Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His  115  120  125  tgg ctc agc gag acc cac agg gcc cta gag gcc atc cgg gat ggc ctc Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu  130  cgc aag ggg acc cac aag gac gtc cta gaa gag gag acc gag agc tcc Arg Lys Gly Thr His Lys Asp Val Leu Glu Gly Gly Thr Glu Ser Ser  155	Thr Gly Leu Glr	Ser Leu Leu	Gln Gly Phe S	ser Arg hearing box -jo	
Cly Asn Leu Leu Arg Gly Ile Asp Ser Leu Phe Leu Cot		20	25	30	302
35       40       350         The Construction of the Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His 50       55       60       350         Cag ctg ggg aac aac aac acc ctc tcc agc cac ctc cag atc gac aag gta 398         Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val 65       75         ccc agg atg gag gag aag gag gag gcc ctg gta ccc atc cag aag gcc acg 446         Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr 80       95         gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc ttc tgg atc att 494         Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile 110         aag ctg cca cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac 110         Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His 125         120         125         tgg ctc agc gag aag cga cac cac cag gac ctc cac cag gac ggc atc cac cag gat ggc ctc cac cag gac gac ctc cac cac cag gac gac ctc cac cac gag gac ctc cac cac gac gac gac ctc cac cac gac gac gac ctc cac cac gac gac ctc cac cac gac gac gac ctc cac gac gac gac cac gac gac cac gac ga	ggt aac ctg ctt	cgg ggc ata	gac agc tta t	the ser ale pro Met Asp	7
ttc cgg ggc ctc cct ggg aac tac cac aaa gag gag aac cag gag cac  Phe Arg Gly Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His  50 55 60  cag ctg ggg aac aac acc ctc tcc agc cac ctc cag atc gac aag gta  Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val  65 70 75  ccc agg atg gag gag aag ggc ctg gta ccc atc cag aag gcc acg  Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr  80 85  gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc ttc tgg atc att  Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile  100 105 110  aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac  Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His  115 120 125  tgg ctc agc gag aag cc cac aag gac gcc atc cgg gat ggc ctc  Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu  130 135  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc ccc  Arg Lys Gly Thr His Lys Asp Val Leu Glu Gly Gly Thr Glu Ser Ser		Arg Gly lie	ASP SET DEU 1	45	
Phe Arg Gly Leu Pro Gly Asn Tyr His Lys Glu Ran Care Care Care Care Care Care Care Care	at	r cct ggg aac	tac cac aaa o	gag gag aac cag gag cac	350
cag ctg ggg aac aac acc ctc tcc agc cac ctc cag atc gac aag gta  Gln Leu Gly Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val  65	Phe Ara Glv Let	u Pro Gly Asn	Tyr His Lys	Glu Glu Asn Gln Glu His	
Gln Leu Gly Asn Asn Thr Leu Ser Ser HIS Leu Gli Tre Asp 2/5 to 65 70 75  ccc agg atg gag gag aag gag gcc ctg gta ccc atc cag aag gcc acg 446  Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr 90 95  gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc ttc tgg atc att 494  Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile 100 105 110  aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac 542  Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His 115 120 125  tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc 590  Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu 130 135 140  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc 638  Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser	E 0		55	80	208
Gln Leu Gly Asn Asn Thr Leu Ser Ser HIS Leu Gli Tre Asp 2/5 to 65 70 75  ccc agg atg gag gag aag gag gcc ctg gta ccc atc cag aag gcc acg 446  Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr 90 95  gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc ttc tgg atc att 494  Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile 100 105 110  aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac 542  Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His 115 120 125  tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc 590  Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu 130 135 140  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc 638  Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser	cag ctg ggg aa	c aac acc ctc	tcc agc cac	ctc cag atc gac aag gta	390
ccc agg atg gag gag aag gag gcc ctg gta ccc atc cag aag gcc acg 446  Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr 80 85 90 95  gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc ttc tgg atc att 494  Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile 100 105 110  aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac 542  Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His 125  tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc 590  Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu 130  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc 638  Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser	Gln Leu Gly As	n Asn Thr Leu	Ser Ser His	Den Giu ite wah ala ima	
Pro Arg Met Glu Glu Lys Glu Ala Leu Val Pro Tie Glu Lys Glu Ala Leu Val Pro Tie Glu Lys Glu Bys Met Glu Glu Lys Glu Ala Leu Val Pro Tie Glu Lys Arg His Arg Leu Glu Glu Gly Gly His Lys Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser Met Glu Glu Gly Gly Thr Glu Ser Ser Leu Gly Gly Thr Glu Ser Ser Leu Glu Gly Gly Thr Glu Ser Ser Leu Gly Gly Thr Glu Ser Ser Leu Glu Gly Gly Thr Glu Ser Ser Leu Glu Glu Gly Gly Thr Glu Ser Ser Leu Glu Glu Glu Gly Thr Glu Ser Ser Leu Glu Glu Glu Gly Thr Glu Ser Ser Leu Glu Glu Glu Gly Thr Glu Ser Ser Leu Glu Glu Glu Glu Glu Glu Glu Glu Glu Gl	65	70	acc cta ata		446
gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc ttc tgg atc att  Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile  100 105 110  aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac  Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His  115 120 125  tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc  Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu  130 135 140  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc  Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser	ccc agg atg ga	g gag aag gag u Glu Lys Glu	Ala Leu Val	Pro Ile Gln Lys Ala Thr	
gac agc ttc cac aca gaa ctc cat ccc cgg gtg gcc ttc tgg atc atc  Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile  100 105 110  aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac  Lys Leu Pro Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His  115 120 125  tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc  Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu  130 135 140  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc  Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser	0.0	95		90	
Asp Ser Phe His Thr Glu Leu His Pro Arg Val Ala Phe 110  100  105  110  aag ctg cca cgg cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac  Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His  115  120  125  tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc  Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu  130  135  140  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc  Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser	++0 03	c aca gaa cto	cat ccc cgg	gtg gcc ttc tgg atc att	494
aag ctg cca cgg agg tcc cac cag gat gcc ctg gag ggc ggc cac  Lys Leu Pro Arg Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His  115  120  125  tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc  Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu  130  135  140  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc  Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser	Asp Ser Phe Hi	s Thr Glu Lev	His Pro Arg	val Ala Phe lip lic li	
Lys Leu Pro Arg Arg Arg Ser His Gin Asp Ala Leu Giu Giy Giy Ala Cigc aag gigg acc cac aag gac gtc cta gaa gag gigg acc gag agc tcc Gig aag gigg acc cac aag gac gtc cta gaa gag gigg acc gag agc tcc Giy Thr His Lys Asp Val Leu Giu Giu Giy Thr Giu Ser Ser		100	105	110	542
tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc  Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu  130  135  140  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc  Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser	aag ctg cca cg	g cgg agg tco	cac cag gar	Ala Leu Glu Gly Gly His	
tgg ctc agc gag aag cga cac cgc ctg cag gcc atc cgg gat gga ctc  Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu  130  135  140  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc  Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser  150  155			120	125	
Trp Leu Ser Glu Lys Arg His Arg Leu Gln Ala 11e Arg Asp Gly Leu  130  135  140  cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc  Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser  150  155	ton ata 255 63	מ שפת כתם כמנ	cac cta caa	gcc atc cgg gat gga ctc	590
cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc 638 Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser	Tro Leu Ser Gl	u Lvs Arg His	Arg Leu Gln	Ala Ile Arg Asp Gly Leu	
cgc aag ggg acc cac aag gac gtc cta gaa gag ggg acc gag agc tcc 638 Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser 150 155	130		135	140	620
Arg Lys Gly Thr His Lys Asp Val Leu Glu Glu Gly III Glu Ser Ser		cc cac aag ga	gtc cta gaa	gag ggg acc gag agc tcc	930
150 150	Arg Lys Gly Th	nr His Lys As	o val Leu Giu	GIM GIA INI GIM PEL PEL	
too can too agg org too our tya any act the tou boy the first	3.45	15	0	100	686
	tee cae tee ag	gg ctg tcc cc	c cya aay acc		

Ser His Ser Arg Leu Ser Pro Arg Lys Thr His Leu Leu Tyr Ile Leu 160 165 170 175 agg ccc tct cgg cag ctg taggggtggg gaccggggag cacctgcctg	734
Arg Pro Ser Arg Gln Leu 180	
tagcccccat cagaccctgc cccaagcacc atatggaaat aaagttcttt c	785
<210> 119	
<211> 559	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	•
<222> 44505	
	•
<221> sig_peptide <222> 44223	
<223> Von Heijne matrix	
score 4	
seq LVRRTLLVAALRA/WM	
-400- 110	
<400> 119 agcaaccaga gggagatgat cacctgaacc actgctccaa acc atg ggc agt aaa	55
Met Gly Ser Lys	
-60	
tgc tgt aaa ggt ggt cca gat gaa gat gca gta gaa aga cag agg cgg	103
Cys Cys Lys Gly Gly Pro Asp Glu Asp Ala Val Glu Arg Gln Arg Arg	
-55 -50 -45 cag aag ttg ctt ctt gca caa ctg cat cac aga aaa agg gtg aag gca	151
Gln Lys Leu Leu Ala Gln Leu His His Arg Lys Arg Val Lys Ala	
-40 -35 -30 -25	
get ggg cag ate cag gee tgg tgg egt ggg gte etg gtg ege agg ace	199
Ala Gly Gln Ile Gln Ala Trp Trp Arg Gly Val Leu Val Arg Arg Thr	
-20 -15 -10 ctg ctg gtt gct gcc ctc agg gcc tgg atg att cag tgc tgg tgg agg	24.7
Leu Leu Val Ala Ala Leu Arg Ala Trp Met Ile Gln Cys Trp Trp Arg	<b>5</b>
-5 1 5	
acg ttg gtg cag aga cgg atc cgt cag cgg cgg cag gcc ctg ttg agg	295
Thr Leu Val Gln Arg Arg Ile Arg Gln Arg Arg Gln Ala Leu Leu Arg	
10 15 20	343
gtc tac gtc atc cag gag cag gcg acg gtc aag ctc cag tcc tgc atc Val Tyr Val Ile Gln Glu Gln Ala Thr Val Lys Leu Gln Ser Cys Ile	243
25 30 35 40	
cgc atg tgg cag tgc cgg caa tgt tac cgc caa atg tgc aat gct ctc	391
Arg Met Trp Gln Cys Arg Gln Cys Tyr Arg Gln Met Cys Asn Ala Leu	
45 50 55	420
tgc ttg ttc cag gtc cca gag agc agc ctt gcc ttc cag act gat ggc	439
Cys Leu Phe Gln Val Pro Glu Ser Ser Leu Ala Phe Gln Thr Asp Gly 60 65 70	
ttt tta cag gtc caa tat gca atc cct tca aag cag cca gag ttc cac	487
Phe Leu Gln Val Gln Tyr Ala Ile Pro Ser Lys Gln Pro Glu Phe His	
75 80 85	
att gaa atc cta tca atc tgaaaggcct ggggcatgga gaacaggctg	535
Ile Glu Ile Leu Ser Ile	
90 Cactacccta ataaatgtct gacc	559
caccaccca acadacyccc yacc	222

```
<210> 120
<211> 770
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 25..393
<221> sig_peptide
<222> 25..150
<223> Von Heijne matrix
     score 4.6
      seq LDPAVSLSAPAFA/SA
<221> polyA_signal
<222> 734..739
 <221> polyA_site
 <222> 757..770
 <400> 120
 cgcagaaagg agagacacac atac atg aaa gga gga gct ttc tcc aat ctt
                            Met Lys Gly Gly Ala Phe Ser Asn Leu
                                    -40
 aat gat too cag oto toa goo tog ttt otg caa ooc ago otg caa goa
                                                                        99
 Asn Asp Ser Gln Leu Ser Ala Ser Phe Leu Gln Pro Ser Leu Gln Ala
                                 -25
             -30
 aac tgt cct gct ttg gac cct gct gtg tca ctc tcc gca cca gcc ttt
                                                                       147
 Asn Cys Pro Ala Leu Asp Pro Ala Val Ser Leu Ser Ala Pro Ala Phe
                                                  -5
                              -10
 ged tot get out ego tot atg aag too too dag get goa egg aag gad
         -15
                                                                       195
 Ala Ser Ala Leu Arg Ser Met Lys Ser Ser Gln Ala Ala Arg Lys Asp
                                          10
 gac ttt ctc agg tct ctt agt gat gga gac tca ggg aca tca gaa cac
                                                                       243
 Asp Phe Leu Arg Ser Leu Ser Asp Gly Asp Ser Gly Thr Ser Glu His
                                      25
                  20
  atc tca gcg gtg gtg act agc cct cgg att tcc tgc cat ggt gct gcc
                                                                        291
  Ile Ser Ala Val Val Thr Ser Pro Arg Ile Ser Cys His Gly Ala Ala
                                  40
              35
  att ccc acc gcc cgt gcc ctc tgc cta ggc tgt tcc tgc tgc acc gaa
                                                                        339
  Ile Pro Thr Ala Arg Ala Leu Cys Leu Gly Cys Ser Cys Cys Thr Glu
                                                   60
                              55
  cgc ctc ctc ctg cca ccg ccc tcc ctc ctt tct tta gaa gcc cct gcc
                                                                        387
  Arg Leu Leu Pro Pro Pro Ser Leu Leu Ser Leu Glu Ala Pro Ala
                          70
  age ace tgagetetet getgattget gtteeteeca gtetgtggaa getttgeeca
                                                                        443
  Ser Thr
  tatgctttcc ttaaaagggt tctgggcagg gcaggcgccc ccatttctca gggatcccct
                                                                        503
  ccaggacaac gccttttcct tgtgtcttca gctctcctta ccagatatct atatatttgt
                                                                         563
  atatattcag tttcaccaac aatgcatcaa gtacttttt ttttaagtaa agaaccgcag
                                                                         623
   tcatcgaact ggagccccat tgattccctc cccctcgcct ccccaaatct ggcacctgcc
                                                                         683
   caaggtatcc tcagaaccat ttggggtgtc ctttggcatt ggataataga aataaaattt
                                                                         743
                                                                         770
   tacctcttc tacaaaaaaa aaaaaac
```

<210> 121 <211> 1213 <212> DNA <213> Homo sapiens WO 99/31236 -96- PCT/IB98/02122

<220> <221> CDS <222> 58..1095 <221> sig\_peptide <222> 58..114 <223> Von Heijne matrix score 5.4 seg LSHLLPSLRQVIQ/EP <221> polyA\_site . <222> 1202..1213 <400> 121 57 cctggctttg cctttgccct gctgtgtgat cttagctccc tgcccaggcc cacagcc 105 atg gcc atg gcc cag aaa ctc agc cac ctc ctg ccg agt ctg cgg cag Met Ala Met Ala Gln Lys Leu Ser His Leu Leu Pro Ser Leu Arg Gln -10 -15 gtc atc cag gag cct cag cta tct ctg cag cca gag cct gtc ttc acg 153 Val Ile Gln Glu Pro Gln Leu Ser Leu Gln Pro Glu Pro Val Phe Thr 201 gtg gat cga gct gag gtg ccg ccc ctc ttc tgg aag ccg tac atc tat Val Asp Arg Ala Glu Val Pro Pro Leu Phe Trp Lys Pro Tyr Ile Tyr 20 249 geg ggc tac egg eeg etg cat eag ace tgg ege tte tat tte ege acg Ala Gly Tyr Arg Pro Leu His Gln Thr Trp Arg Phe Tyr Phe Arg Thr 35 40 297 ctg ttc cag cag cac aac gag gcc gtg aat gtc tgg acc cac ctg ctg Leu Phe Gln Gln His Asn Glu Ala Val Asn Val Trp Thr His Leu Leu 50 gcg gcc ctg gta ctg ctg ctg cgg ctg gcc ctc ttt gtg gag acc gtg 345 Ala Ala Leu Val Leu Leu Leu Arg Leu Ala Leu Phe Val Glu Thr Val 393 gac ttc tgg gga gac cca cac gcc ctg ccc ctc ttc atc att gtc ctt Asp Phe Trp Gly Asp Pro His Ala Leu Pro Leu Phe Ile Ile Val Leu 80 85 441 que tet tte ace tac etc tec etc agt gee ttg get cac etc etg cag Ala Ser Phe Thr Tyr Leu Ser Leu Ser Ala Leu Ala His Leu Leu Gln 100 105 gcc aag tot gag tto tgg cat tac agc tto tto ctg gac tat gtg 489 Ala Lys Ser Glu Phe Trp His Tyr Ser Phe Phe Phe Leu Asp Tyr Val 120 115 ggg gtg gcc gtg tac cag ttt ggc agt gcc ttg gca cac ttc tac tat 537 Gly Val Ala Val Tyr Gln Phe Gly Ser Ala Leu Ala His Phe Tyr Tyr 130 135 585 gct atc gag ccc gcc tgg cat gcc cag gtg cag gct gtt ttt ctg ccc Ala Ile Glu Pro Ala Trp His Ala Gln Val Gln Ala Val Phe Leu Pro 150 atg gct gcc ttt ctc gcc tgg ctt tcc tgc att ggc tcc tgc tat aac 633 Met Ala Ala Phe Leu Ala Trp Leu Ser Cys Ile Gly Ser Cys Tyr Asn 160 aag tac atc cag aaa cca ggc ctg ctg ggc cgc aca tgc cag gag gtg 681 Lys Tyr Ile Gln Lys Pro Gly Leu Leu Gly Arg Thr Cys Gln Glu Val 180 729 ccc tcc gtc ctg gcc tac gca ctg gac att agt cct gtg gtg cat cgt Pro Ser Val Leu Ala Tyr Ala Leu Asp Ile Ser Pro Val Val His Arg 205 190 195 777 atc ttc gtg tcc tcc gac ccc acc acg gat gat cca gct ctt ctc tac Ile Phe Val Ser Ser Asp Pro Thr Thr Asp Asp Pro Ala Leu Leu Tyr

215

825

WO 99/31236 -97- PCT/IB98/02122 -

His Lys Cys Gln Val Val Phe Phe Leu Leu Ala Ala Phe Phe Ser	
225 230 235	873
acc ttc atg ccc gag cgc tgg ttc cct ggc agc tgc cat gtc ttc ggg Thr Phe Met Pro Glu Arg Trp Phe Pro Gly Ser Cys His Val Phe Gly 240 245 250	075
cag ggc cac caa ctt ttc cat atc ttc ttg gtg ctg tgc acg ctg gct Gln Gly His Gln Leu Phe His Ile Phe Leu Val Leu Cys Thr Leu Ala	921
255 260 265	060
cag ctg gag gct gtg gca ctg gac tat gag gcc cga cgg ccc atc tat Gln Leu Glu Ala Val Ala Leu Asp Tyr Glu Ala Arg Arg Pro Ile Tyr	969
270 275 280 285	1017
gag cct ctg cac acg cac tgg cct cac aac ttt tct ggc ctc ttc ctg Glu Pro Leu His Thr His Trp Pro His Asn Phe Ser Gly Leu Phe Leu	
290 295 300 ctc acg gtg ggc agc atc ctc act gca ttc ctc ctg agc cag ctg	1065
Leu Thr Val Gly Ser Ser Ile Leu Thr Ala Phe Leu Leu Ser Gln Leu	
gta cag cgc aaa ctt gat cag aag acc aag tgaaggggga tggcatctgg	1115
Val Gln Arg Lys Leu Asp Gln Lys Thr Lys 320 325	•
tagggaggga ggtatagttg ggggacaggg gtctgggttt ggctccaagt gggaacaagg	1175 1213
cctggtaaag ttgtttgtgt ctggccaaaa aaaaaaaa	,1213
<210> 122	
<211> 1318	
<213> Homo sapiens	•
<220>	
<221> CDS	
<222> 31660	
<221> sig_peptide <222> 3190	
<223> Von Heijne matrix	
score 5.4 seg AFVIACVLSLIST/IY	
<221> polyA_signal	
<222> 12881293	
<221> polyA site	
<222> 13071318	
<400> 122	- 4
ggaggatggg cgagcagtct gaatgccaga atg gat aac cgt ttt gct aca gca Met Asp Asn Arg Phe Ala Thr Ala -20	54
ttt gta att gct tgt gtg ctt agc ctc att tcc acc atc tac atg gca	102
Phe Val Ile Ala Cys Val Leu Ser Leu Ile Ser Thr Ile Tyr Met Ala -10 -5 1	
get tee att gge aca gae tte tgg tat gag tat ega agt eea gtt caa	150
Ala Ser Ile Gly Thr Asp Phe Trp Tyr Glu Tyr Arg Ser Pro Val Gln 5 10 15 20	
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser	198
25 30 35	
gat gag gca gat gaa aag act tat aat gat gca ctt ttt cga tac aat Asp Glu Ala Asp Glu Lys Thr Tyr Asn Asp Ala Leu Phe Arg Tyr Asn	246
40 45 50	

ggc Gly	aca Thr	Val	gga Gly	ttg Leu	tgg Trp	aga Arg	cgg Arg 60	tgt Cys	atc Ile	acc Thr	ata Ile	ccc Pro 65	aaa Lys	aac Asn	atg Met	<b>294</b>
cat His	tgg Trp 70	55 tat Tyr	agc Ser	cca Pro	cca Pro	gaa Glu 75	agg	aca Thr	gag Glu	tca Ser	ttt Phe 80	gat	gtg Val	gtc Val	aca Thr	342
Lys 85	tgt Cys	Val	agt Ser	Phe	Thr 90	Leu	Thr	Glu	Gln	Phe 95	.Met	Glu	Lys	Phe	Val 100	390
Asp	Pro	Gly	aac Asn	His 105	Asn	Ser	Gly	Ile	Asp 110	Leu	Leu	Arg	Thr	Tyr 115	Leu	438
Trp	Arg	Cys	cag Gln 120	Phe	-Leu	Leu	Pro	Phe 125	Val	Ser	Leu	Gly	Leu 130	Met	Cys	486
ttt Phe	ggg Gly	gct Ala 135	ttg Leu	atc Ile	gga Gly	ctt Leu	tgt Cys 140	Ala	tgc Cys	att Ile	tgc Cys	cga Arg 145	Ser	tta Leu	tat .Tyr	534
ccc Pro	acc Thr 150	att Ile	gcc Ala	acg Thr	ggc Gly	att Ile 155	ctc Leu	cat His	ctc Leu	ctt Leu	gca Ala 160	Val	aca Thr	Lys	gag Glu	582
agc Ser 165	atg Met	ctt Leu	cca Pro	gct Ala	gga Gly 170	gct Ala	gag Glu	tcc Ser	aag Lys	cac His 175	Thr	gcc Ala	act Thr	cct Pro	gca Ala 180	630
			gtg Val		Thr					•	gaga	aga	ggaa	agag	igt	680
tgt	aggg	att	tggg	aaga	ac c	ttga	ttat	t cc	ctgg	agga	aaa	gaca	aat	ctac	ttccct	740
gaa	atca	CCC	tcga	atct	ac t	tcca	ccct	c ag	aact	taaa	atg	aact	gca	tttc	tttttt	800 860
cat	cttc	ttt	CCCC	CTCC	ag t	gaat	atga		ccaa	acco	cto	toac	aag	atga	gaactgt aaaattg	920
aad	cctc	tta	ttat	aaaa	tt c	acct	aget	a as	ctca	qqaa	acc	agge	aag	aagt	caatgc	980
agg	catt	taa	aatq	taaa	gt t	tttt	ctgg	jt ta	aato	tatt	tat	ttt	ctt	gtag	ggttgag	1040
tat	ttct	tcc	cagt	tttt	ct g	ctct	ggtg	t at	aaca	aaca	i ggt	caaa	att	tccc	catcttt	1100
cct	cctg	ata	gtag	ttga	at c	ctac	ctte	c at	actt	aato	cat	agt	gaaa	tgg	catctag	1160
cag	aaat	aca	cacc	ccca	aa a	caca	ccac	c at	ttca	ttag	gts	ccca	aaaa	aatt	ctgtat	1220
											cca	ectat	tata	ttga	actgcaa	1280 1318
acg	aatt	aat	aaat	tato	CC T	.נכני	yaaa	ad di	adadā	add						2220

```
<210> 123
```

<213> Homo sapiens

<220>

<221> CDS

<222> 31..582

<221> sig\_peptide

<222> 31..90

<223> Von Heijne matrix score 5.4 seq AFVIACVLSLIST/IY

<221> polyA\_signal

<222> 816..821

<221> polyA\_site

<222> 840..853

<sup>&</sup>lt;211> 853

<sup>&</sup>lt;212> DNA

<pre>&lt;400&gt; 123 ggaggatggg cgagcagtct gaatgccaga atg gat aac cgt ttt gct aca gca</pre>	54
ttt gta att gct tgt gtg ctt agc ctc att tcc acc atc tac atg gca Phe Val Ile Ala Cys Val Leu Ser Leu Ile Ser Thr Ile Tyr Met Ala	102
gcc tcc att ggc aca gac ttc tgg tat gaa tat cga agt cca gtt caa Ala Ser Ile Gly Thr Asp Phe Trp Tyr Glu Tyr Arg Ser Pro Val Gln	150
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser	198
gat gaa gca gat gaa aag act tat aat gat gca cct ttt cga tac aat	246
ggc aca gtg gga ttg tgg aga cgg tgt atc acc ata ccc aaa aac atg	294
cat tgg tat agc cca cca gaa agg aca gag tca ttt gat gtg gtc aca His Trp Tyr Ser Pro Pro Glu Arg Thr Glu Ser Phe Asp Val Val Thr	342
aaa tgt gtg agt ttc aca cta act gag cag ttc atg gag aaa ttt gtt Lys Cys Val Ser Phe Thr Leu Thr Glu Gln Phe Met Glu Lys Phe Val	390
gat ccc gga aac cac aat agc ggg att gat ctc ctt agg acc tat ctt Asp Pro Gly Asn His Asn Ser Gly Ile Asp Leu Leu Arg Thr Tyr	438
tgg cgt tgc cag ttc ctt tta cct ttt gtg agt tta ggt ttg tgc Trp Arg Cys Gln Phe Leu Leu Pro Phe Val Ser Leu Gly Leu Met Cys	486
ttt ggg gct ttg atc gga ctt tgt gct tgc att tgc cga agc tta tat  Phe Gly Ala Leu Ile Gly Leu Cys Ala Cys Ile Cys Arg Ser Leu Tyr	534
ccc acc att gcc acg ggc att ctc cat ctc ctt gca gat acc atg ctg Pro Thr Ile Ala Thr Gly Ile Leu His Leu Leu Ala Asp Thr Met Leu	582
150 155 1600 1500 1500 1500 1500 1500 15	642 702
gctccaact gacagccaac atcatttcca gccatgtgtg ggagccatcc tggatgtcca gccttaacaa gccttcagag gacttcagcc acagctatta tcttactaca tccttgtgag actctaataa agaaccaact agctgagccc aatcaaccta tggaactgat agaaataaaa tgaattgttg ttttgcgaaa aaaaaaaaaa	

<210> 124

<211> 826

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 15..695

<221> sig\_peptide

<222> 15..80

<223> Von Heijne matrix score 8.5 seq AALLLGLMMVVTG/DE

<221> polyA\_signal

<222> 795..800

<221> polyA\_site <222> 814..826

<400> 124 aaccagaggt gccc atg ggt tgg aca atg agg ctg gtc aca gca gca ctg 50 Met Gly Trp Thr Met Arg Leu Val Thr Ala Ala Leu -20 tta ctg ggt ctc atg atg gtg gtc act gga gac gag gat gag aac agc 98 Leu Leu Gly Leu Met Met Val Val Thr Gly Asp Glu Asp Glu Asn Ser - 5 ccg tgt gcc cat gag gcc ctc ctg gac gag gac acc ctc ttt tgc cag 146 Pro Cys Ala His Glu Ala Leu Leu Asp Glu Asp Thr Leu Phe Cys Gln 15 ggc ctt gaa gtt ttc tac cca gag ttg ggg aac att ggc tgc aag gtt 194 Gly Leu Glu Val Phe Tyr Pro Glu Leu Gly Asn Ile Gly Cys Lys Val 30 gtt cct gat tgt aac aac tac aga cag aag atc acc tcc tgg atg gag 242 Val Pro Asp Cys Asn Asn Tyr Arg Gln Lys Ile Thr Ser Trp Met Glu , , , . 45 ccg ata gtc aag ttc ccg ggg gcc gtg gac ggc gca acc tat atc ctg 290 Pro Ile Val Lys Phe Pro Gly Ala Val Asp Gly Ala Thr Tyr Ile Leu 60 65 gtg atg gtg gat cca gat gcc cct agc aga gca gaa ccc aga cag aga 338 Val Met Val Asp Pro Asp Ala Pro Ser Arg Ala Glu Pro Arg Gln Arg 80 ttc tgg aga cat tgg ctg gta aca gat atc aag ggc gcc gac ctg aag 386 Phe Trp Arg His Trp Leu Val Thr Asp Ile Lys Gly Ala Asp Leu Lys 90 5 6 95 aaa ggg aag att cag ggc cag gag tta tca gcc tac cag gct ccc tcc 434 Lys Gly Lys Ile Gln Gly Gln Glu Leu Ser Ala Tyr Gln Ala Pro Ser 110 cca ccg gca cac agt ggc ttc cat cgc tac cag ttc ttt gtc tat ctt 482 Pro Pro Ala His Ser Gly Phe His Arg Tyr Gln Phe Phe Val Tyr Leu cag gaa gga aag gtc atc tct ctc ctt ccc aag gaa aac aaa act cga 530 Gln Glu Gly Lys Val Ile Ser Leu Leu Pro Lys Glu Asn Lys Thr Arq 140 145 ggc tct tgg aaa atg gac aga ttt ctg aac cgt ttc cac ctg ggc gaa 578 Gly Ser Trp Lys Met Asp Arg Phe Leu Asn Arg Phe His Leu Gly Glu cet gaa gea age ace eag tte atg ace eag aac tae eag gae tea eea 626 Pro Glu Ala Ser Thr Gln Phe Met Thr Gln Asn Tyr Gln Asp Ser Pro 170 175 acc ctc cag gct ccc aga gaa agg gcc agc gag ccc aag cac aaa aac 674 Thr Leu Gln Ala Pro Arg Glu Arg Ala Ser Glu Pro Lys His Lys Asn 190 195 cag gcg gag ata gct gcc tgc tagatagccg gctttgccat ccgggcatgt 725 Gln Ala Glu Ile Ala Ala Cys 205 ggccacactg cccaccaccg acgatgtggg tatggaaccc cctctggata cagaacccct 785 826

<sup>&</sup>lt;210> 125

<sup>&</sup>lt;211> 571

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;220>

<sup>&</sup>lt;221> CDS

<222> 74295	
<221> sig_peptide	•
<222> 74196	
<223> Von Heijne matrix	
score 5.4	
seq RLLYIGFLGYCSG/LI	
<221> polyA_signal	•
<221> polyA_site	
<222> 561571	
<400> 125	60
cgggtagtgg tcgtcgtggt tttccttgta gttcgtggtc tgagaccagg cctcaagtgg	.60 109
aaacggcgtc acc atg atc gca cgg cgg aac cca gta ccc tta cgg ttt Met Ile Ala Arg Arg Asn Pro Val Pro Leu Arg Phe	103
-40 -35 -30	
ctg ccg gat gag gcc cgg agc ctg ccc ccg ccc aag ctg acc gac ccg	157
Leu Pro Asp Glu Ala Arg Ser Leu Pro Pro Pro Lys Leu Thr Asp Pro	
-25 -20 -15	
cgg ctc ctc tac atc ggc ttc ttg ggc tac tgc tcc ggc ctg att gat	205
Arg Leu Leu Tyr Ile Gly Phe Leu Gly Tyr Cys Ser Gly Leu Ile Asp	
-10 -5 1 aac ctg atc cgg cgg agg ccg atc gcg acg gct ggt ttg cat cgc cag	253
Asn Leu Ile Arg Arg Pro Ile Ala Thr Ala Gly Leu His Arg Gln	
5 10 15	
ctt cta tat att acg gcc ttt ttt ttg ctg gat att atc ttg	295
Leu Leu Tyr Ile Thr Ala Phe Phe Leu Leu Asp Ile Ile Leu	
20 25 30	355
taaaacgtga agactacctg tatgctgtga gggaccgtga aatgtttgga tatatgaaat	415
tacatccaga ggattttcct gaagaagata agaaaacata tggtgaaatt tttgaaaaat tccatccaat acgttgaagt cttcaaaatg cttgctccag tttcactgat acctgctgtt	475
cctgaatttg atggaacatg tttcttatga cagttgaagc ttatgctaat ctgtatgttg	535
acaccttgta attaaaatac gtaccaaaaa aaaaaa	571
<210> 126	
<211> 659 <212> DNA	
<212> DNA <213> Homo sapiens	
<220>	
<221> CDS	
<222> 440658	
<221> polyA_signal	
<222> 601606	
<400> 126	
caccttacaa actaggaagat gatgeetete acceagetaa ttgeteteta geeettagee	60
ttcacaggiq tiggigeetg cegigaaege atteigaeet gggeegiate igieteeeaa	120
gactttgtgc ctatggttgg ggacagagtg aggtcgttgc cttgacgacg acagcatgcg	180 240
gcccgtggtc ctcctaagtg tgagcttgcg gcggaccgag gcccacctgc ctccctgcct	300
gettegecca ggaetegtga etgegteege agaagaaate acaacagege tggaattget	360

Met Glu Lys Tyr Glu Asn Leu Gly Leu Val Gly 5

agtttgctag gcagcatctt ttggacctgc gaaccatatg catttcacct caaatctgtt

tccaagttga aaacctttgg gtctttctat gcgaacggat tgaagaaacg caaaaagttt

ctacggactt taaattaaa atg gaa aaa tat gaa aac ctg ggt ttg gtt gga

360

420

gaa ggg agt tat gga atg gtg atg aag tgt agg aat aaa gat act gga

520

Glu Gly Ser	Tyr Gly Me	t Val Met Ly 20	s Cys Arg Asn	Lys Asp Thr Gly 25	
aga att gtg Arg Ile Val 30	gcc ata aa Ala Ile Ly	g aag ttc tt s Lys Phe Le 35	a gaa agt gac u Glu Ser Asp		568
gtt aaa aag Val Lys Lys 45	att gca at Ile Ala Me	g cga gaa gt t Arg Glu Va 50	c aag tta cta l Lys Leu Leu 55		616
cat gaa aac His Glu Asn 60	ttg gtg aa Leu Val As 65	t ctc ttg ga n Leu Leu Gl	a gtg tgt aaa u Val Cys Lys 70	aaa aaa a Lys Lys	659
<210> 127 <211> 301	٠.,			e e e	••
<212> DNA <213> Homo	sapiens				
<220> <221> CDS <222> 382	83		" , " " " " "	e e e e e e e e e e e e e e e e e e e	
<221> sig_po <222> 3889 <223> Von Ho score	5 eijne matri				
<221> polyA <222> 257	_signal	·			
<400> 127					
cacctgaatc (	ccaggaaccc	tcaatgaggt c		g aga ctg ctg cca s Arg Leu Leu Pro s	55
gct acc agc Ala Thr Ser -10	ctg gct gg Leu Ala Gl -5	c cct gtc ct y Pro Val Le	g tcc acc ctc u Ser Thr Leu 1	att gcc cca act Ile Ala Pro Thr	103
ccc atg ttg Pro Met Leu	ttt tgt ga Phe Cys Gl 10	a gat aaa ag u Asp Lys Se 15	r Trp Asp Leu	ttt ctt ttt ttt Phe Leu Phe Phe 20	151
aag tct cac Lys Ser His 25	aag aca tg Lys Thr Tr	g ggc atc tc	c aca aat tta		199
Phe Gly Asn	Leu Phe Le	u Cys Val Gl 45	n Phe Val Arg 50	Glu Lys Gln Ser	247
ttt tgt atg Phe Cys Met 55	aat aca ga Asn Thr Gl 60	a tgt gat tt u Cys Asp Le	a cgc aag aat u Arg Lys Asn 65	tgacaaaaa	293
aaaaaaa					301

<210> 128

<211> 477

<212> DNA

<213> Homo sapiens

<221> CDS <222> 121..477 <221> sig\_peptide <222> 121..288 <223> Von Heijne matrix score 3.5 seg SSCADSFVSSSSS/OP <400> 128 cctcggagca ggcggagtaa agggacttga gcgagccagt tgccggatta ttctatttcc 60 cetecetete tecegeceeg tatetettt caccettete ceaccetege tegegtagee 120 atg gcg gag ccg tcg gcg gcc act cag tcc cat tcc atc tcc tcg tcg 168 Met Ala Glu Pro Ser Ala Ala Thr Gln Ser His Ser Ile Ser Ser Ser -55 -50 tcc ttc gga gcc gag ccg tcc gcg ccc ggc ggc ggc ggg agc cca gga 216 . Ser Phe Gly Ala Glu Pro Ser Ala Pro Gly Gly Gly Ser Pro Gly -40 -35 gcc tgc ccc gcc ctg ggg acg aag agc tgc agc tcc tcc tgt gcg gat . 264 Ala Cys Pro Ala Leu Gly Thr Lys Ser Cys Ser Ser Ser Cys Ala Asp -20 -15 tee ttt gtt tet tee tet tee tet cag eet gta tet eta ttt teg ace 312 Ser Phe Val Ser Ser Ser Ser Ser Gln Pro Val Ser Leu Phe Ser Thr - 5 tca caa gag gga ttg agc tct ctt tgc tct gat gag cca tct tca gaa 360 Ser Gln Glu Gly Leu Ser Ser Leu Cys Ser Asp Glu Pro Ser Ser Glu 15 20 att atg act tct tcc ttt ctt tca tct tct gaa ata cat aac act ggc 408 Ile Met Thr Ser Ser Phe Leu Ser Ser Ser Glu Ile His Asn Thr Gly 25 30 35 ctt aca ata cta cat gga gaa aaa agc cat gtg tta ggg agc cag cct 456 Leu Thr Ile Leu His Gly Glu Lys Ser His Val Leu Gly Ser Gln Pro 45 50 att tta gcc aaa aaa aaa aaa 477 Ile Leu Ala Lys Lys Lys 60 <210> 129 <211> 323 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 2..163 <221> polyA signal <222> 292..297 <221> polyA\_site <222> 310..323 <400> 129 a gct ttc gtg tgg gag cca gct atg gtg cgg atc aat gcg ctg aca gca Ala Phe Val Trp Glu Pro Ala Met Val Arg Ile Asn Ala Leu Thr Ala gcc tct gag gct gcg tgc ctg atc gtg tct gta gat gaa acc atc aag 97

Ala Ser Glu Ala Ala Cys Leu Ile Val Ser Val Asp Glu Thr Ile Lys 20 25 30 aac ccc cgc tcg act gtg gat gct ccc aca gca gca ggc cgg ggc cgt

WO 99/31236 -104- PCT/IB98/02122 -

Asn Pro Arg Ser Thr Val Asp Ala Pr	ro Thr Ala Ala Gly Arg Gly Arg	
ggt cgt ggc cgc ccc cac tgagaggcac Gly Arg Gly Arg Pro His 50	c cccacccatc acatggctgg	193
ctggctgctg ggtgcactta ccctccttgg cagtaattggc ccactctctt cttactggag gaaaaaaaaaa		253 313 323
••		
<210> 130		
<211> 1392		
<212> DNA		
<213> Homo sapiens		. •
<220>	•	
<221> CDS	·	
<222> 46675	•	
2223 pig nontido		
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 4687</pre>		
<223> Von Heijne matrix		
score 5.3		
seq LTLLGLSFILAGL/IV		
<221> polyA_signal		
<222> 13641369	p.t.	
<221> polyA_site <222> 13831392		
• •		
<400> 130		
<pre>&lt;400&gt; 130 ctccgagttg ccacccagga aaaagagggc</pre>		57
	Met Leu Thr Leu	57 105
ctccgagttg ccacccagga aaaagagggc tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc ly Leu Ile Val Gly Gly Ala Cys	
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc ly Leu Ile Val Gly Gly Ala Cys 1 5	105
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc ly Leu Ile Val Gly Gly Ala Cys 1 5 gc acc att tac cgt gga gag atg	
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc ly Leu Ile Val Gly Gly Ala Cys 1 5 gc acc att tac cgt gga gag atg	105
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc Gly Leu Ile Val Gly Gly Ala Cys 1 5 gc acc att tac cgt gga gag atg Ger Thr Ile Tyr Arg Gly Glu Met 5 20 gca aat tcc ctt cgt gga gga gag	105
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc Gly Leu Ile Val Gly Gly Ala Cys 1 5 gc acc att tac cgt gga gag atg Ger Thr Ile Tyr Arg Gly Glu Met 5 20 gca aat tcc ctt cgt gga gga gag Ala Asn Ser Leu Arg Gly Gly Glu	105 153
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 gca aat tcc ctt cgt gga gga gag ala Asn Ser Leu Arg Gly Gly Glu 35	105 153 201
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 gca aat tcc ctt cgt gga gga gag ala Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac	105 153
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 ga aat tcc ctt cgt gga gga gag gla Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac glu Ala Asp Ile Arg Glu Asp Asp 50	105 153 201
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G aac att gca atc att gat gtg cct g aac att gca atc att gat gtg cct g	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 gca aat tcc ctt cgt gga gga gag gla Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac glu Ala Asp Ile Arg Glu Asp Asp 50 gtc ccc agt ttc tct gat agt gac	105 153 201
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro Val	Met Leu Thr Leu  ga ctt att gtt ggt gga gcc tgc  ly Leu Ile Val Gly Gly Ala Cys  1 5  ggc acc att tac cgt gga gag atg  ger Thr Ile Tyr Arg Gly Glu Met  20  gca aat tcc ctt cgt gga gga gag  Ala Asn Ser Leu Arg Gly Gly Glu  35  gag gct gac att cgt gag gat gac  Slu Ala Asp Ile Arg Glu Asp Asp  50  gtc ccc agt ttc tct gat agt gac  Val Pro Ser Phe Ser Asp Ser Asp	105 153 201 249
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro Val 55 60	Met Leu Thr Leu  ga ctt att gtt ggt gga gcc tgc  ly Leu Ile Val Gly Gly Ala Cys  1 5  ggc acc att tac cgt gga gag atg  ger Thr Ile Tyr Arg Gly Glu Met  20  gca aat tcc ctt cgt gga gga gag  Ala Asn Ser Leu Arg Gly Gly Glu  35  gag gct gac att cgt gag gat gac  Slu Ala Asp Ile Arg Glu Asp Asp  50  gtc ccc agt ttc tct gat agt gac  Val Pro Ser Phe Ser Asp Ser Asp  65	105 153 201 249
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro Val	Met Leu Thr Leu  ga ctt att gtt ggt gga gcc tgc  ly Leu Ile Val Gly Gly Ala Cys  1 5  ggc acc att tac cgt gga gag atg  ger Thr Ile Tyr Arg Gly Glu Met  20  gca aat tcc ctt cgt gga gga gag  Ala Asn Ser Leu Arg Gly Gly Glu  35  gag gct gac att cgt gag gat gac  Slu Ala Asp Ile Arg Glu Asp Asp  50  gtc ccc agt ttc tct gat agt gac  7al Pro Ser Phe Ser Asp Ser Asp  65  70  gaa aag gga atg act gct tac ctg	105 153 201 249 297
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G 40 45 aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro Val 55 60 cct gca gca att att cat gac ttt g Pro Ala Ala Ile Ile His Asp Phe G	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 gaa aat tcc ctt cgt gga gga gag ala Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac glu Ala Asp Ile Arg Glu Asp Asp 50 gtc ccc agt ttc tct gat agt gac yal Pro Ser Phe Ser Asp Ser Asp 65 gaa aag gga atg act gct tac ctg glu Lys Gly Met Thr Ala Tyr Leu 80	105 153 201 249 297 345
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G 40 45 aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro V 55 60 cct gca gca att att cat gac ttt g Pro Ala Ala Ile Ile His Asp Phe G 75 gac ttg ttg ctg ggg atc tgc tat	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 gga aat tcc ctt cgt gga gga gag gla Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac glu Ala Asp Ile Arg Glu Asp Asp 50 gtc ccc agt ttc tct gat agt gac glu Pro Ser Phe Ser Asp Ser Asp 65 gaa aag gga atg act gct tac ctg glu Lys Gly Met Thr Ala Tyr Leu 80 85 etg atg ccc ctc aat act tct att	105 153 201 249 297
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G 40 45 aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro V 55 60 cct gca gca att att cat gac ttt g Pro Ala Ala Ile Ile His Asp Phe G 75 gac ttg ttg ctg ggg atc tgc tat cat gac ttg ttg ctg ggg atc tgc tat cat gac ttg Leu Leu Leu Gly Ile Cys Tyr I	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 gca aat tcc ctt cgt gga gga gag gla Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac glu Ala Asp Ile Arg Glu Asp Asp 50 gtc ccc agt ttc tct gat agt gac glu Pro Ser Phe Ser Asp Ser Asp 65 gaa aag gga atg act gct tac ctg glu Lys Gly Met Thr Ala Tyr Leu 80 gtg atg ccc ctc aat act tct att Leu Met Pro Leu Asn Thr Ser Ile	105 153 201 249 297 345
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G 40 45 aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro V 55 60 cct gca gca att att cat gac ttt g Pro Ala Ala Ile Ile His Asp Phe G 75 gac ttg ttg ctg ggg atc tgc tat c Asp Leu Leu Leu Gly Ile Cys Tyr I	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 ga aat tcc ctt cgt gga gga gag gala Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac glu Ala Asp Ile Arg Glu Asp Asp 50 gtc ccc agt ttc tct gat agt gac gala Pro Ser Phe Ser Asp Ser Asp 65 gaa aag gga atg act gct tac ctg glu Lys Gly Met Thr Ala Tyr Leu 80 gtg atg ccc ctc aat act tct att Leu Met Pro Leu Asn Thr Ser Ile 95	105 153 201 249 297 345
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G 40 45 aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro V 55 60 cct gca gca att att cat gac ttt g Pro Ala Ala Ile Ile His Asp Phe G 75 gac ttg ttg ctg ggg atc tgc tat cat gac ttg ttg ctg ggg atc tgc tat cat gac ttg Leu Leu Leu Gly Ile Cys Tyr I	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 ga aat tcc ctt cgt gga gga gag gla Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac glu Ala Asp Ile Arg Glu Asp Asp 50 gtc ccc agt ttc tct gat agt gac glu Ala Asp Ile Arg Glu Asp Asp 50 gtc ccc agt ttc tct gat agt gac glu Pro Ser Phe Ser Asp Ser Asp 65 gaa aag gga atg act gct tac ctg glu Lys Gly Met Thr Ala Tyr Leu 80 gtg atg ccc ctc aat act tct att Leu Met Pro Leu Asn Thr Ser Ile 95 gag ctc ttt ggc aaa ctg gcg agt	105 153 201 249 297 345 393
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G 40 45 aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro Val S5 60 cct gca gca att att cat gac ttt g Pro Ala Ala Ile Ile His Asp Phe G 75 gac ttg ttg ctg ggg atc tgc tat c Asp Leu Leu Leu Gly Ile Cys Tyr I 90 gtt atg cct cca aaa aat ctg gta g Val Met Pro Pro Lys Asn Leu Val C	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 20 gaa aat tcc ctt cgt gga gga gag gla Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac glu Ala Asp Ile Arg Glu Asp Asp 50 gtc ccc agt ttc tct gat agt gac gal Pro Ser Phe Ser Asp Ser Asp 65 gaa aag gga atg act gct tac ctg glu Lys Gly Met Thr Ala Tyr Leu 80 gtg atg ccc ctc aat act tct att Leu Met Pro Leu Asn Thr Ser Ile 100 gag ctc ttt ggc aaa ctg gcg agt Glu Leu Phe Gly Lys Leu Ala Ser 115	105 153 201 249 297 345 393
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G 40 45 aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro Val 55 60 cct gca gca att att cat gac ttt g Pro Ala Ala Ile Ile His Asp Phe G 75 gac ttg ttg ctg ggg atc tgc tat c Asp Leu Leu Gly Ile Cys Tyr I 90 gtt atg cct cca aaa aat ctg gta g Val Met Pro Pro Lys Asn Leu Val G ggc aga tat ctg cct caa act tat g	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 ga aat tcc ctt cgt gga gga gag gla Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac glu Ala Asp Ile Arg Glu Asp Asp 50 gtc ccc agt ttc tct gat agt gac gla Pro Ser Phe Ser Asp Ser Asp 65 gaa aag gga atg act gct tac ctg glu Lys Gly Met Thr Ala Tyr Leu 80 gtg atg ccc ctc aat act tct att Leu Met Pro Leu Asn Thr Ser Ile 100 gag ctc ttt ggc aaa ctg gcg agt Glu Leu Phe Gly Lys Leu Ala Ser 115 gtg gtt cga gaa gac cta gtt gct	105 153 201 249 297 345 393
tta ggc ctt tca ttc atc ttg gca g Leu Gly Leu Ser Phe Ile Leu Ala G -10 -5 att tac aag tac ttc atg ccc aag a Ile Tyr Lys Tyr Phe Met Pro Lys S 10 1 tgc ttt ttt gat tct gag gat cct g Cys Phe Phe Asp Ser Glu Asp Pro A 25 30 cct aac ttc ctg cct gtg act gag g Pro Asn Phe Leu Pro Val Thr Glu G 40 45 aac att gca atc att gat gtg cct g Asn Ile Ala Ile Ile Asp Val Pro Val S5 60 cct gca gca att att cat gac ttt g Pro Ala Ala Ile Ile His Asp Phe G 75 gac ttg ttg ctg ggg atc tgc tat c Asp Leu Leu Leu Gly Ile Cys Tyr I 90 gtt atg cct cca aaa aat ctg gta g Val Met Pro Pro Lys Asn Leu Val C	Met Leu Thr Leu ga ctt att gtt ggt gga gcc tgc gly Leu Ile Val Gly Gly Ala Cys 1 5 ggc acc att tac cgt gga gag atg ger Thr Ile Tyr Arg Gly Glu Met 5 ga aat tcc ctt cgt gga gga gag gla Asn Ser Leu Arg Gly Gly Glu 35 gag gct gac att cgt gag gat gac glu Ala Asp Ile Arg Glu Asp Asp 50 gtc ccc agt ttc tct gat agt gac gla Pro Ser Phe Ser Asp Ser Asp 65 gaa aag gga atg act gct tac ctg glu Lys Gly Met Thr Ala Tyr Leu 80 gtg atg ccc ctc aat act tct att Leu Met Pro Leu Asn Thr Ser Ile 100 gag ctc ttt ggc aaa ctg gcg agt Glu Leu Phe Gly Lys Leu Ala Ser 115 gtg gtt cga gaa gac cta gtt gct	105 153 201 249 297 345 393

· 150

537 .

135	-0-
ctt tgc aat aac aga aag tcc ttc cgc ctt cgt cgc aga gac ctc ttg	585
Leu Cys Asn Asn Arg Lys Ser Phe Arg Leu Arg Arg Arg Asp Leu Leu	
155 160 165	
100	633
ctg ggt ttc aac aaa cgt gcc att gat aaa tgc tgg aag att aga cac	000
Leu Gly Phe Asn Lys Arg Ala Ile Asp Lys Cys Trp Lys Ile Arg His	
170 175 180	
ttc ccc aac gaa ttt att gtt gag acc aag atc tgt caa gag	675
Phe Pro Asn Glu Phe Ile Val Glu Thr Lys Ile Cys Gln Glu	
103	725
taagaggcaa cagatagagt gtccttggta ataagaagtc agagatttac aatatgactt	735
taacattaag gtttatggga tactcaagat atttactcat gcatttactc tattgcttat	795
gctttaaaaa aaggaaaaaa aaaaaactac taaccactgc aagctcttgt caaattttag	855
tttaattggc attgcttgtt ttttgaaact gaaattacat gagtttcatt ttttctttgc	915
titalitys attitude to the same and the same	975
atttataggg tttagatttc tgaaagcagc atgaatatat cacctaacat cctgacaata	1035
aattocator gttgtttttt ttgtttgttt gttttttttt ttcctttaag taagctcttt	
Affigition togginged detectuates togginates tourseless	1095
ttgtgtaaaa tatatcagat ctcaacattg ttggtttctt ttgtttttca ttttgtacaa	1155
ctttcttgaa tttagaaatt acatctttgc agttctgtta ggtgctctgt aattaacctg	1215
Citients and the control of the cont	1275
acttatatgt gaacaatttt catgagacag tcatttttaa ctaatgcagt gattctttct	
cactactate tgtattgtgg aatgeacaaa attgtgtagg tgetgaatge tgtaaggagt	1335
ttaggttgta tgaattctac aaccctataa taaattttac tctatacaaa aaaaaaa	1392
<210> 131 <211> 999 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 62385	:
<221> polyA_signal <222> 974979	;
<221> polyA_site	
<222> 987999	
4005 121	
<400> 131	60
cctgaatgac ttgaatgttt ccccgcctga gctaacagtc catgtgggtg attcagctct	
g atg gga tgt gtt ttc cag agc aca gaa gac aaa tgt ata ttc aag ata	109
Met Gly Cys Val Phe Gln Ser Thr Glu Asp Lys Cys Ile Phe Lys Ile	
10	
1	157
gac tgg act ctg tca cca gga gag cac gcc aag gac gaa tat gtg cta	157
Asp Trp Thr Leu Ser Pro Gly Glu His Ala Lys Asp Glu Tyr Val Leu	
20 25 30	
tac tat tac tcc aat ctc agt gtg cct att ggg cgc ttc cag aac cgc	205
tal tal tal tal tal and tal an	
Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg	
35 40 45	
gta cac ttg atg ggg gac atc tta tgc aat gat ggc tct ctc ctg ctc	253
Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly Ser Leu Leu Leu	
50 55 60	
caa gat gtg caa gag gct gac cag gga acc tat atc tgt gaa atc cgc	403
544 545 545 544 545 544 544 544 544 544	301
Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg	301
Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg	301
Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg 65 70 75 80	
Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg	349

90

85

95

gtg gag gaa att cgt gat gtt agt aac ctt ggc atc ttt att tac caa Val Glu Glu Ile Arg Asp Val Ser Asn Leu Gly Ile Phe Ile Tyr Gln

140

ctt cca gag gag ccc aaa ggt acg caa atg ctt act taaagagggg

395 '

Leu Pro Glu Glu Pro Lys Gly Thr Gln Met Leu Thr  100 105	
ccaaggggca agagctttca tgtgcaagag gcaaggaaac tgattatctt gagtaaatgc cagcctttgg gctaagtact taccacagag tgaatcttca aaaaatgatc ataattatt cagtcaataa aaatagagtt attttattaa ataaaatatt gataattatt gtattattac	455 515 575
tttaaacaca cttcccctc acaaaagccc tgtgaaggat gttttgttca catatatgtc	635
caaatatgtt ttggacacat atttattaaa tggaataaat agtacttgaa ccctggcacc	695
totgacaaca aagtocatgt totttttact atgoodtaat acctttcatc agttatocac	755
attgatgcta catctgtatt ttataggtac cctatgttag gtgttctggg ggatagaaaa	815
gaaataagca ggccaggctc agtggctcat gcctgtaatc ctagcatttt gggaggctga	875
ggcagcagaa ctgcctgagc cccagggttc aagactgcag tgagctatga tggcaccact gcattctagc ctgggtgaca gagcaagact ctgtctaaaa taaaaaaaag gaaaaaaaaa	935 995
aaaa	999
	·. ·
<210> 132	
<211> 725 <212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 422550	
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 422475</pre>	
<pre>&lt;222&gt; 422475 &lt;223&gt; Von Heijne matrix</pre>	•
score 4.5	
seq LRWLMPVIPALWG/AE	
<221> polyA_site	
<222> 714725	
<400> 132	
tctgcgaggg tgggagagaa aattaggggg agaaaggaca gagagagcaa ctaccatcca	60
tagccagata ggtgagtaaa tatatttgca gtaacctatt tgctattcct tgctgcaact	120
gtgtttaatg ttccttccag aatcagagag agtattgcca tccaagaaat cgtttttaga	180
tatgacattt gagctatcat cttgagacca atacctaaaa caatttcagt ttaagaaatg tctaggtatg gtgaaaacac agtttaaaac cagcaaaaca gaatttattg ccctcagcga	240 300
atacccacaa tgtacatata ccttgtattt ctgaaagcaa agcaagcatg ccaagtagtt	360
tttatttacc tgtacctata atacagcaag gtgaaacagg atatatttt gaagtttaaa	420
a atg tct tca ggc cgg ctg cgg tgg ctc atg cct gta atc cca gca ctt	469
Met Ser Ser Gly Arg Leu Arg Trp Leu Met Pro Val Ile Pro Ala Leu -15 -10 -5	
tgg gga gcc gag aag ggt gaa tca cct gag gtc agc agt ttt gag acc	517
Trp Gly Ala Glu Lys Gly Glu Ser Pro Glu Val Ser Ser Phe Glu Thr	
1 5 10	
agg ctg gcc aac atg gcg aaa ccc tgt ctc tac tgaaaataca aaaattagct	570
Arg Leu Ala Asn Met Ala Lys Pro Cys Leu Tyr 15 20 25	
15 20 25 999tgtgggtg gegggegeet gtagteecag etaettggga gaetgaggea ggagaattge	630
ttgaacacgg aaggcggaag ttgcagtaag ctgagatcgt gccaccgcac accagcttgg	690
gcaacagagt gagactooot otcaaaaaaa aaaaa	725

<sup>&</sup>lt;210> 133

<sup>&</sup>lt;211> 400

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Homo sapiens

<220	>		'e1													
<221			,											•		
<222	> 12	42	. 31													
<221	> po	lyA_	site	<b>:</b>												
<222	> 38	74	00													٠
<400	> 13	3								•						
															tagaa	60
															ctctg	120
_	Met								Lys					att : Ile :		168
	1	tct	acc	ata	_	cct	cat	+++			atc	acc	+++	gta		216
								Phe						Val :		
acc	ttt	ttc	caa	ata	tagt	cact	ct c	tgag	gtac	t ga	tggt	tagg	atc	tcaa	cat	271
Thr	Phe	Phe	Gln 35	Ile												•
acct	tttt	tg g	gagg	acac	a at	tgaa	ccca	taa	cagg	gtg	tttg	caag	ga a	gagt	taaaa	331
tttg	aaag	aa a	ggtg	gtat	t to	ctta	gata	gat	aggg	cac	agct	ttct	ag g	tgac	aaaaa	391
aaaa	aaaa	.a								•						400
<210	> 13	4														
<211	> 10	53														
<212				1												•
<213	> Ho	mo s	apie	ens												
<220	-															
<221		s														
<222	> 13	1	051													
		_	ptid	ie												
<222			ios eijne	mat	rix											
1223		ore	_													
	se	q MI	IRVSI	TVPI	LGA/	MM										
		_		_												
	•		sign													
<222	:> 1(	119	1024	ł												
<400	)> 13	34														
			gacgo	gcts	gc ga	acago	gccg	ged	ccto	gegg	ccgc	aggt	cg t	caca	gacga	60
															cgagt	120
gaco	ttct													gga g		169
		ı	set 1	seu A		/al 8 -10	ser 1	eu 1	inr v		-5	.eu 1	.eu (	Gly P	11a	
ato	ato	cta	cta	gaa			ata	gat	cca		_	ctc	agc	ttc	aaa	217
														Phe		
1				5				-	10					15	-	
														ctg		265
Glu	Pro	Pro		Leu	Leu	Gly	Val		His	Pro	Asn	Thr	_	Leu	Arg	
Car	ac =	<b>C</b> 22	20	ctc	+++	G 2 2	22+	25 Caa	ctt	a++	aa.	000	30	tcc	ate	313
														Ser		J 1.
		35	ن				40				3	45			-	
														cgg		36:
Ala	His	Ile	Gly	Asp	Val	Met	Phe	Thr	Gly	Thr	Ala	Asp	Gly	Arg	Val	

gta Val	aaa Lvs	Ctt Leu	gaa Glu	aat Asn	ggt Glv	gaa Glu	ata Ile	gag	acc Thr	att	gcc	cgg	ttt	ggt	tcg Ser		409
65					70					75					80		•.
											tgt						457
				85					90		Сув			95			
ggt	atc	cgt	gca	999	ccc	aat	999	act	ctc	ttt	gtg	gcc	gat	gca	tgc		505
			100	,				105	,		Val		110				
aag	gga	cta	ttt	gaa	gta	aat	ccc	tgg	aaa	cgt	gaa	ġtg	aaa	ctg	ctg		553
Lys	Gly	Leu 115	Phe.	Glu	Val	Asn	Pro 120		Lys	Arg	Glu.	Val 125	Lys	Leu	Leu		
ctg	tcc	tcc	gag	aca	ccc	att	gag	999	aag	aac	atg	tcc	ttt	gtg	aat		601
Leu	Ser	Ser	Glu	Thr	Pro	Ile	Glu	Gly	Lys	Asn	Met	Ser	Phe	Val	Asn		
	130					135					140					7	
gat	ctt	aca	gtc	tct	cag	gat	999	agg	aag	att	tat	ttc	acc	gat	tct		649
	Leu	Thr	Val	Ser		Asp	Gly	Arg	Lys	Ile	Tyr	Phe	Thr	Asp.	Ser		
145					150					155					160		
											ctg						697
				165					170		Leu			175	_		,
aca	gat	gac	999	cgc	ctg	ctg	gag	tat	gat	act	gtg	acc	agg	gaa	gta		745
Thr	Asp	Asp		Arg	Leu	Leu	Glu		Asp	Thr	Val	Thr		Glu	Val	:	
			180					185					190		:		
aaa	gtt	tta	ttg	gac	cag	ctg	caa	ttc	ccg	aat	gga	gtc	cag	ctg	tct		793
		195					200			7 (	Gly	205					
cct	gca	gaa	gac	ttt	gtc	ctg	gtg	gca	gaa	aca	acc	atg	gcc	agg	ata		841
	210					215					Thr 220						
cga	aga	gtc	tac	gtt	tct	ggc	ctg	atg	aag	ggc	999	gct	gat	ctg	ttt		889
Arg	Arg	Val	Tyr	Val		Gly	Leu	Met	Lys	Gly	Gly	Ala	Asp	Leu	Phe		
225					230					235					240		
gtg	gag	aac	atg	cct	gga	ttt	cca	gac	aac	atc	cgg	ccc	agc	agc	tct		937
val	GIU	Asn	Met		GIÀ	Phe	Pro	qaA		Ile	Arg	Pro	Ser		Ser		
		<b>.</b>	<b>.</b>	245					250					255			
999	999	Tac	rgg	grg	ggc	atg	tcg	acc	atc	cgc	cct	aac	cct	999	ttt		985
Gly	GTA	IYI		vaı	GIÀ	met	ser		TIE	Arg	Pro	Asn		GIĀ	Phe		
tcc	ato	ctc	260	++-	++-	+ = +	~~~	265					270				3000
Ser	Met	Len	yar Aer	Dhe	Len	Cer	gay	aya aya	Dec	rgg	att Ile	aaa	agg	acg	act Tla		1033
		275					280	AIG	PIO	пр	116	ьуs 285	Arg	met	116		
		gca				aa											1053
rne		Ala	тÀв	гàг	гàг												
	290							•									•

<210> 135

<211> 1128

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 86..403

<221> sig\_peptide

<222> 86..181

<223> Von Heijne matrix score 8.8 seq VPMLLLIVGGSFG/LR

```
<221> polyA_signal
  <222> 1097..1102
  <221> polyA_site
  <222> 1117..1128
  <400> 135
                                                                         60
  cgtcttggtg agagcgtgag ctgctgagat ttgggagtct gcgctaggcc cgcttggagt
  tctgagccga tggaagagtt cactc atg ttt gca ccc gcg gtg atg cgt gct
                                                                        112
                              Met Phe Ala Pro Ala Val Met Arg Ala
                                                           -25
                                       -30
                                                                        160
  ttt cgc aag, aac aag act ctc ggc tat gga gtc ccc atg ttg ttg ctg
... Phe Arg Lys Asn Lys Thr Leu Gly Tyr Gly Val Pro Met Leu Leu Leu
               -20
                                   -15
                                                                        208
att gtt gga ggt tot ttt ggt ott ogt gag ttt tot caa ato oga tat
  Ile Val Gly 3ly Ser Phe Gly Leu Arg Glu Phe Ser Gln Ile Arg Tyr
          - 5
                                                                        256
  gat gct gtg aag agt aaa atg gat cct gag ctt gaa aaa aaa ctg aaa
  Asp Ala Val Lys Ser Lys Met Asp Pro Glu Leu Glu Lys Lys Leu Lys
                      15
                                           20
                                                                        304
  gag aat aaa ata tot tta gag tog gaa tat gag aaa ato aaa gac too
  Glu Asn Lys Ile Ser Leu Glu Ser Glu Tyr Glu Lys Ile Lys Asp Ser
                   30
                                                                        352
  aag ttt gat gac tgg aag aat att cga gga ccc agg cct tgg gaa gat
  Lys Phe Asp Asp Trp Lys Asn Ile Arg Gly Pro Arg Pro Trp Glu Asp
                                   50
              45
                                                                        400
  cct gac ctc ctc caa gga aga aat cca gaa agc ctt aag act aag aca
  Pro Asp Leu Leu Gln Gly Arg Asn Pro Glu Ser Leu Lys Thr Lys Thr
                               65
                                                   70
  act tgactctgct gattcttttt tccnnntttt tttttttta aataaaaata
                                                                        453
  ctattaactg gacttcctaa tatatacttc tatcaagtgg aaaggaaatt ccaggcccat
                                                                         573
  ggaaacttgg atatgggtaa tttgatgaca aataatcttc actaaaggtc atgtacaggt
                                                                         633
  ttttatactt cccagctatt ccatctgtgg atgaaagtaa caatgttggc cacgtatatt
                                                                         693
  ttacacctcg aaataaaaaa tgtgaatact gctccaaaaa aaaaaaccag taccgtgtag
                                                                         753
  tctctctcgt ggcttggatt tacactgggc aacgtggttg gaatgtatct ggctcagaac
  tatgatatac caaacctggc taaaaaactt gaagaaatta aaaaggactt ggatgccaag
                                                                         813
                                                                         873
  aagaaacccc ctagtgcatg agactgcctc cagcactgcc ttcaggatat accgattcta
  ctgctcttga gggcctcgtt tactatctga accaaaagct tttgttttcg tctccagcct
                                                                         933
  cagcacttct cttctttgct agaccctgtg ttttttgctt taaagcaagc aaaatggggc
                                                                         993
  cccaatttga gaactacccg acgtttccaa catactcacc tcttcccata atccctttcc
                                                                        1053
  aactgcatgg gaggttctaa gactggaatt atggtgctag attagtaaac atgactttta
                                                                        1113
   acgaaaaaaa aaaaa
                                                                        1128
```

<210> 136 <211> 254

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 37..162

<221> sig\_peptide

<222> 37..93

<223> Von Heijne matrix scoxe 9.5 seg LMCLSLCTAFALS/KP

<221> polyA_signal <222> 224229	•.
<221> polyA_site <222> 243254	
<400> 136 tgtgctgtgg gggctacgag gaaagatcta attatc atg gac ctg cga cag ttt Met Asp Leu Arg Gln Phe	54
-15 ctt atg tgc ctg tcc ctg tgc aca gcc ttt gcc ttg agc aaa ccc aca Leu Met Cys Leu Ser Leu Cys Thr Ala Phe Ala Leu Ser Lys Pro Thr -10 -5	102
gaa aag aag gac cgt gta cat cat gag cct cag ctc agt gac aag gtt Glu Lys Lys Asp Arg Val His His Glu Pro Gln Leu Ser Asp Lys Val 5 10 15	150
cac aat gat att tgatagaacc aattgttgta cataaaacag atctgcgcat His Asn Asp Ile 20	202
atatatatat gtataaaaaa taataaaata atggaagatg aaaaaaaa	<b>254</b>
<210> 137	
<211> 886	
<212> DNA <213> Homo sapiens	
<220>	
<221> CDS	
<222> 31381	
<221> sig_peptide	
<222> 3190	
score 5.4	
seq AFVIACVLSLIST/IY	•
<221> polyA_site <222> 875886	
<400> 137	
ggaggatggg cgagcagtct gaatggcaga atg gat aac cgt ttt gct aca gca Met Asp Asn Arg Phe Ala Thr Ala -20 -15	54
ttt gta att gct tgt gtg ctt agc ctc att tcc acc atc tac atg gca Phe Val Ile Ala Cys Val Leu Ser Leu Ile Ser Thr Ile Tyr Met Ala -10 -5	102
gcc tcc att ggc aca gac ttc tgg tat gaa tat cga agt cca gtt caa	150
Ala Ser Ile Gly Thr Asp Phe Trp Tyr Glu Tyr Arg Ser Pro Val Gln 5 10 15 20	
	198
gaa aat too agt gat ttg aat aaa ago ato tgg gat gaa tto att agt	
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser	
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser 25 30 35 gat gag gca gat gaa aag act tat aat gat gca ctt ttt cga tac aat	246
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser 25 30 35	246
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser 25 30 35 gat gag gca gat gaa aag act tat aat gat gca ctt ttt cga tac aat Asp Glu Ala Asp Glu Lys Thr Tyr Asn Asp Ala Leu Phe Arg Tyr Asn 40 45 50 ggc aca gtg gga ttg tgg gga cgg tgt atc acc ata ccc aaa aac atg	246 294
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser 25 30 35 gat gag gca gat gaa aag act tat aat gat gca ctt ttt cga tac aat Asp Glu Ala Asp Glu Lys Thr Tyr Asn Asp Ala Leu Phe Arg Tyr Asn 40 45 50	
gaa aat tcc agt gat ttg aat aaa agc atc tgg gat gaa ttc att agt Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser 25 30 35  gat gag gca gat gaa aag act tat aat gat gca ctt ttt cga tac aat Asp Glu Ala Asp Glu Lys Thr Tyr Asn Asp Ala Leu Phe Arg Tyr Asn 40 45 50  ggc aca gtg gga ttg tgg gga cgg tgt atc acc ata ccc aaa aac atg Gly Thr Val Gly Leu Trp Gly Arg Cys Ile Thr Ile Pro Lys Asn Met	

70 75 80 tot gtc ttc acc tgg tta ata ata gac aaa acg acg taatgattgc	391
Ser Val Phe Phe Thr Trp Leu Ile Ile Asp Lys Thr Thr 85 90 95	•,
ccaattacat gtaagcaggt ttgttggttc tctctctct taaagaaata aatcgtgtat	451 511
cttetette tactgeette tetececaae ttetttgeat taccatggta etcateaata ttggttggat gaggaaettt tettatettg ggaaageett aatggetttt tttttetta	571
tttactcact cattaaaata cttttcatta ctctaacaca tgttataaag aaatagttgg	631
aaaaqtqcat cgaaaqactt ttaaaaaatat ttggtaacta gtaaaaggac taccatcgaa	691
aatcaactca aaaaattgtc cttttatggg ttagctgtat tataatacat atctatcatt	751
tgcccctgtg tcttagagga tataatttga ccagctctac atttaatctg tgtaattatg agactgtttt acaacaatct tgatgcagag ttggtaggtt aagaaatttg tattacagaa	811 871
qttaaaaaaa aaaaa	886
20000000000000000000000000000000000000	•
	· .
<210> 138	
<211> 1244	•
<212> DNA <213> Homo sapiens	
2213> NOMO Bapiens	
<220>	•
<221> CDS	
<222> 46579	
<221> sig_peptide	
<222> 46156	
<223> Von Heijne matrix	
score 3.5	
seq LVFNFLLILTILT/IW	•
<400> 138	
cccttatcca ggttnttatc tanggaatcc cnnnaagact gggga atg gag aga cag Met Glu Arg Gln -35	
Met Glu Arg Gln -35 tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna	
Met Glu Arg Gln -35 tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa	
Met Glu Arg Gln -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa -30 -25 -20	105
Met Glu Arg Gln -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa -30 -25 -20  qcg qng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg	
Met Glu Arg Gln -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa -30 -25 -20  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu -15 -10 -5	105
Met Glu Arg Gln -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa -30 -25 -20  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu -15 -10 -5 aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act	105
Met Glu Arg Gln  -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa  -30  -25  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu  -15  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr	105 153
Met Glu Arg Gln  -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa  -30  -25  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu  -15  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr  1  1  1  1  1  1  1  1  1  1  1  1  1	105 153 201
Met Glu Arg Gln -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa -30 -25 -20  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu -15 -10 -5  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr 1 5 10 15 16 17 17 18 18 18 18 18 18 18 18 18 18 18 18 18	105 153
Met Glu Arg Gln -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa -30  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu -15  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr 1  gga gga gca atg gtg tat ggc ctt ata atg gga cta att tca cga tat Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu Ile Ser Arg Tyr 20  Met Glu Arg Gln -35  Leu can nna cat cat can nna cat cat cat cat cat ctt acc att ttg -20  10  15  15  10  15  15  16  17  18  18  19  20  25  30	105 153 201 249
Met Glu Arg Gln  -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa  -30  -25  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu  -15  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr  1  gga gga gca atg gtg tat ggc ctt ata atg gga cta att tca cga tat Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu Ile Ser Arg Tyr  20  gct aca gca cca act gat att gaa agt gga act gtc tgt gac tgt gta	105 153 201
Met Glu Arg Gln  -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa  -30  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu  -15  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr  1  gga gga gca atg gtg tat ggc ctt ata atg gga cta att tca cga tat Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu Ile Ser Arg Tyr  20  gct aca gca cca act gat att gaa agt gga act gtc tgt gac tgt gta Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Thr Val Cys Asp Cys Val	105 153 201 249
Met Glu Arg Gln  -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa  -30  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu  -15  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr  1  gga gga gca atg gtg tat ggc ctt ata atg gga cta att tca cga tat Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu Ile Ser Arg Tyr  20  gct aca gca cca act gat att gaa agt gga act gtc tgt gac tgt gta Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Thr Val Cys Asp Cys Val  35	105 153 201 249
Met Glu Arg Gln  -35  tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa  -30  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu  -15  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr  1  gga gga gca atg gtg tat ggc ctt ata atg gga cta att tca cga tat Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu Ile Ser Arg Tyr  20  gct aca gca cca act gat att gaa agt gga act gtc tgt gac tgt gta Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Thr Val Cys Asp Cys Val	105 153 201 249 297
tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna  Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa  -30 -25 -20  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg  Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu  -15 -10 -5  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act  Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr  1 5 10 15  gga gga gca atg gtg tat ggc ctt ata atg gga cta att tca cga tat  Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu Ile Ser Arg Tyr  20 25 30  gct aca gca cca act gat att gaa agt gga act gtc tgt gac tgt gta  Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Thr Val Cys Asp Cys Val  35 40 45  aaa cta act ttc agt cca cca act ctg ctg gtt aat gtc act gac caa  Lys Leu Thr Phe Ser Pro Pro Thr Leu Leu Val Asn Val Thr Asp Gln	105 153 201 249 297
tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna  Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa  -30 -25 -20  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg  Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu  -15 -10 -5  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act  Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr  1 5 10 15  gga gga gca atg gtg tat ggc ctt ata atg gga cta att tca cga tat  Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu Ile Ser Arg Tyr  20 25 30  gct aca gca cca act gat att gaa agt gga act gtc tgt gac tgt gta  Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Thr Val Cys Asp Cys Val  35 40 45  aaa cta act ttc agt cca cca act ctg ctg gtt aat gtc act gac caa  Lys Leu Thr Phe Ser Pro Pro Thr Leu Leu Val Asn Val Thr Asp Gln  50 55 60  gtt tat gaa tat aaa tac aaa aga gaa ata agt cag cac aac atc aat	105 153 201 249 297
tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna  Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa  -30 -25 -20  gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu  -15 -10 -5  aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr  1 5  gga gga gca atg gtg tat ggc ctt ata atg gga cta att tca cga tat Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu Ile Ser Arg Tyr  20 25 30  gct aca gca cca act gat att gaa agt gga act gtc tgt gac tgt gta Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Thr Val Cys Asp Cys Val  35  aaa cta act ttc agt cca cca act ctg ctg gtt aat gtc act gac caa Lys Leu Thr Phe Ser Pro Pro Thr Leu Leu Val Asn Val Thr Asp Gln  50  gtt tat gaa tat aaa tac aaa aga gaa ata agt cag cac aac atc aat Val Tyr Glu Tyr Lys Tyr Lys Arg Glu Ile Ser Gln His Asn Ile Asn	105 153 201 249 297
Met Glu Arg Gln	105 153 201 249 297
Met Glu Arg Gln	105 153 201 249 297 345
Met Glu Arg Gln	105 153 201 249 297 345 393
tca agg gtt atg tca gaa aag gat gag tat cag ttt caa cat can nna Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe Gln His Xaa Xaa -30 gcg gng gan ctg ctt gtc ttc aat ttt ttg ctc atc ctt acc att ttg Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile Leu Thr Ile Leu -15 aca atc tgg tta ttt aaa aat cat cga ttc cgc ttc ttg cat gaa act Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr 1 gga gga gca atg gtg tat ggc ctt ata atg gga cta att tca cga tat Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu Ile Ser Arg Tyr 20 gct aca gca cca act gat att gaa agt gga act gtc tgt gac tgt gta Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Thr Val Cys Asp Cys Val 35 aaa cta act tc agt cca cca act ctg ctg gtt aat gtc act gac caa Lys Leu Thr Phe Ser Pro Pro Thr Leu Leu Val Asn Val Thr Asp Gln 50 gtt tat gaa tat aaa tac aaa aga gaa ata agt cag cac aac atc aat Val Tyr Glu Tyr Lys Tyr Lys Arg Glu Ile Ser Gln His Asn Ile Asn 65 cct cat caa gga aat gct ata ctt gaa aag atg aca ttt gat cca gaa Pro His Gln Gly Asn Ala Ile Leu Glu Lys Met Thr Phe Asp Pro Glu 80 atc ttc ttc aat gtt tta ctg cca cca att ata ttt cat gca gga tat atc ttc ttc aat gtt tta ctg cca cca att ata ttt cat gca gga tat atc ttc ttc aat gtt tta ctg cca cca att ata ttt cat gca gga tat atc ttc ttc aat gtt tta ctg cca cca att ata ttt cat gca gga tat atc ttc ttc aat gtt tta ctg cca cca att ata ttt cat gca gga tat atc ttc ttc aat gtt tta ctg cca cca att ata ttt cat gca gga tat	105 153 201 249 297 345
Met Glu Arg Gln	105 153 201 249 297 345 393

WO 99/31236 -112- PCT/IB98/02122

115 120 125	537 
tat gcc ttc ttg gga act gcc atc tcc tgc atc gtc ata ggg Tyr Ala Phe Leu Gly Thr Ala Ile Ser Cys Ile Val Ile Gly 130 135 140	579
taagtgacat teggagetea agttgeaggt ggetgtgggg tetgtgatet gtgtgaggga tetaacactt ceaggattet tgetggetgg gaaaattgte tttttttag tatateacat atttgtatgt tttttetgac ttaatteeac ggettetgac aaatacaagg etteaaatea aggaateact tgeettgagt tatgtgaage geattgett ggaettetga ettagggaat gtggateact tgeettgagt tatgtgaage geattgeat ettetttag tttgagtaat geegatatgg teactgeatt etttttgte ttgtattgag agaeeettaee tgtatttgge aggagtgeaa aagtaactat atgeeaagag ttttettet aaaggaaagt ttaeaagaca geagtetgaa acagatatgn teeaaatatn naacagagtt gettaataca gggatagett tteagttaat accetgtaga atgeagacee tttnttteat tgtatttet tgattatget actgageeet aagteacacg ttatataete tggettgeag eteaataca agtaaaatgt ggtaecaaat ggtgaaggea ateeageetn tgataateee gteeaataca ttaaagntee actge	639 699 759 819 879 939 999 1059 1119 1239 1244
<210> 139 <211> 471 <212> DNA <213> Homo sapiens	-
<220> <221> CDS <222> 92469	
<221> sig_peptide <222> 92172 <223> Von Heijne matrix     score 7.9     seq VVVLALGFLGCYG/AK	
<221> polyA_signal <222> 454459	
<222> 454459  <221> polyA_site <222> 458471  <400> 139 gcaagtgcag aagtcggtga cggtgggcat ctgggtgtca atcgatgggg catcctttct gaagatcttc gggccactgt cgtccagtgc c atg cag ttt gtc aac gtg ggc Met Gln Phe Val Asn Val Gly -25	60 112
<pre>&lt;222&gt; 454459  &lt;221&gt; polyA_site &lt;222&gt; 458471  &lt;400&gt; 139 gcaagtgcag aagtcggtga cggtgggcat ctgggtgtca atcgatgggg catcettet gaagatette gggccactgt cgtccagtge c atg cag ttt gte aac gtg ggc</pre>	
<pre>&lt;222&gt; 454459  &lt;221&gt; polyA site &lt;222&gt; 458471  &lt;400&gt; 139 gcaagtgcag aagtcggtga cggtgggcat ctgggtgtca atcgatgggg catcctttct gaagatcttc gggccactgt cgtccagtgc c atg cag ttt gtc aac gtg ggc</pre>	112
<pre>&lt;222&gt; 454459  &lt;221&gt; polyA_site &lt;222&gt; 458471  &lt;400&gt; 139 gcaagtgcag aagtcggtga cggtgggcat ctgggtgtca atcgatgggg catcettet gaagatette gggccactgt cgtccagtge c atg cag ttt gte aac gtg ggc</pre>	112
<pre>&lt;222&gt; 454459  &lt;221&gt; polyA_site &lt;222&gt; 458471  &lt;400&gt; 139 gcaagtgcag aagtcggtga cggtgggcat ctgggtgtca atcgatgggg catcettet gaagatette gggccactgt cgtccagtge c atg cag ttt gtc aac gtg ggc</pre>	112 160 208

•																
caa Gln	gtg Val	tgg Trp	aac Asn	acc Thr 65	acc Thr	atg Met	aaa Lys	ggg Gly	ctc Leu 70	aag Lys	tgc Cys	cgt Arg	ggc Gly	ttc Phe 75	acc Thr	400
aac Asn	tat Tyr	acg Thr	gat Asp 80	ttt	gag Glu	gac Asp	tca Ser	ccc Pro 85	tac	ttc Phe	aaa Lys	atg Met	cat His 90	aaa Lys	cct Pro	448
-		atg Met	aaa				aa									471
		95		•												
'<213			•	•					•							
<213	3> Ho	omo s	apie	ens									•			,
	1> CI	DS 546	575 <sub>.</sub>													
<222	2 > 1	ig_pe 544 on He	198		rix					,			•			
	S	core eg PI	4.8			/GV				,						
	_	olyA_ 19								•		•				
		olyA_ 38		е												
ccc	atca	ctc (	aggt	tctc	tt c	aact	ccct	c tt	cagt	gcct	act	atgt	tgc	attt	aacca ctccc	c 120
ctg	tgtt	ttg 1	tgaa	gagt	ac c	cagt	acta	t ga	c ate Me -1	t Ar	c tg g Tr	g to p Se	a tg r Cy	s Gl	g cac u His .10	174
ctc Leu	gtt Val	atg Met	gtg Val -10	Trp	atc Ile	aat Asn	gct Ala	ttt Phe -10	Val	atg Met	ctc Leu	acc Thr	acg Thr	Glr	ctg Leu	222
Leu	Pro	Ser -90	aaa Lys	tac Tyr	Cys	Asp	Leu -85	Leu	His	Lys	Ser	Ala -80	a Ala )	His	ctg Leu	270
Gly	Lys -75	Trp	Gln	Lys	Leu	Glu -70	His	Gly	Ser	Tyr	Ser -65	Asr	n Ala	Pro	cag Gln	318
His	; Ile	Trp	Ser	Glu	Asn -55	Thr	Ile	Trp	Pro	Gln -50	Gly	/ Val	Lei	ı Va	g cgg l Arg -45	366
His	s Ser	Arg	Cys	Leu -40	Tyr	Arg	Ala	Met	Gly -35	Pro	туг	Ası	ı Val	1 Ala	-	414
ect	tca Ser	gat Asp	gta Val	Ser	cat His	gcc Ala	cgo Arg	ttt Phe -20	Туг	ttc Phe	tta Lei	tti Phe	t cat e His	s Ar	a cca g Pro	462
tta Lev	a ago	ctg Leu -10	Leu	aat Asn	cto Lev	cto Lev	: ato : Ile -5	ctt Leu	att Ile	gag Glu	g ggo	gg Gl;	t gte y Val	c gt l Va	c ttc l Phe	510
tat Ty:	t cag r Gli	cto	tat	tcc Ser	tto Lei	g cto 1 Lei	cg Arg	g tcg g Ser	g gag Glu	aag Lys	g tgg s Trp	g aa o As:	c ca n Hi	c ac s Th	a ctt r Leu	558

5			1221		10					15					20	
tcc	atg	gct	ctc	atc	ctc	ttc	tgc	aac	tac	tat	gtt	tta	ttt	aaa	ctt	606
Ser	Met	Ala	Leu	Ile	Leu	Phe	Cys	Asn	Tyr	Tyr	Val	Leu	Phe	Lys	Leu	•
				25					30					35		
ctc	cgg	gac	aga	ata	gta	tta	ggc	agg	gca	tac	tcc	tac	cca	ctc	aac	654
Leu	Arg	Asp	Arg	Ile	Val	Leu	Gly	Arg	Ala	Tyr	Ser	Tyr	Pro	Leu	Asn	
			40					45					50			
agt	tat	gaa	ctc	aag	gca	aac	taag	gctg	cct (	ctcaa	acaat	tg ag	ggga	gaact	t.	705
Ser	Tyr	Glu	Leu	.Lys	Ala	Asn										
		55										٠,				
cagataaaaa tattttcata cgttctattt ttttcttgtg atttttataa atatttaaga											765					
tgti	tta	tat 1	tttgi	tata	ct at	tate	gttti	t' gaa	aagt	cggg	aaga	agtaa	agg g	gatai	ttaaat	825
gtatccgtaa acaaaaaaa aaaa												849				

<210> 141 <211> 155 <212> PRT

<213> Homo sapiens ...

<220>

<221> SIGNAL

<222> -31..-1

## <400> 141

Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser
-30 -25 -20

Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu
-15 -5 1

Leu Leu Pro His Cys Gln Lys Pro Phe Val Tyr Asp Leu His Ala Val 5 10 15

Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys 20 25 30

Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe 35 40 45

Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu 50 60 65

Leu Gly Thr Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Glu

Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser 85 90 95

Gly Leu Ile Phe Cys Cys Ala Phe Cys Ser Glu Thr Lys Leu Phe Leu 100 105 110

Ser Arg Gln Ala Met Ala Glu Asn Phe Ser Ile 115 120

<210> 142

<211> 55

<212> PRT

<213> Homo sapiens

## <400> 142

Met Ala Asp Phe Tyr Lys Glu Phe Leu Ser Lys Asn Phe Gln Lys Arg 1 5 10 15

Met Tyr Tyr Asn Arg Asp Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe 20 25 30

Phe Met Gly Lys Val Ala Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln

Lys Gln Lys Lys Arg Ser Asn

1.1

50

55

<210> 143 <211> 67 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -20..-1 ...<400> 143 Met Ser Arg Asn Leu Arg Thr Ala Leu Ile Phe Gly Gly Phe Ile Ser -10 -15 Leu Ile Gly Ala Ala Phe Tyr Pro Ile Tyr Phe Arg Pro Leu Met Arg Leu Glu Glu Tyr Lys Lys Glu Gln Ala Ile Asn Arg Ala Gly Ile Val 20 Gln Glu Asp Val Gln Pro Pro Gly Leu Lys Val Trp Ser Asp Pro Phe Gly Arg Lys 45 <210> 144 <211> 198 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -21..-1 <400> 144 Met Pro Val Pro Ala Leu Cys Leu Leu Trp Ala Leu Ala Met Val Thr -15 Arg Pro Ala Ser Ala Ala Pro Met Gly Gly Pro Glu Leu Ala Gln His 1 Glu Glu Leu Thr Leu Leu Phe His Gly Thr Leu Gln Leu Gly Gln Ala 20 Leu Asn Gly Val Tyr Arg Thr Thr Glu Gly Trp Leu Thr Lys Ala Arg 35 Asn Ser Leu Gly Leu Tyr Gly Arg Thr Ile Glu Leu Leu Gly Gln Glu Val Ser Arg Gly Arg Asp Ala Ala Gln Glu Leu Arg Ala Ser Leu Leu Glu Thr Gln Met Glu Glu Asp Ile Leu Gln Leu Gln Ala Glu Ala Thr 85 Ala Glu Val Leu Gly Glu Val Ala Gln Ala Gln Lys Val Leu Arg Asp 100 Ser Val Gln Arg Leu Glu Val Gln Leu Arg Ser Ala Trp Leu Gly Pro 115 120 Ala Tyr Arg Glu Phe Glu Val Leu Lys Ala His Ala Asp Lys Gln Ser 130 135

His Ile Leu Trp Ala Leu Thr Gly His Val Gln Arg Gln Arg Glu

Met Val Ala Gln Gln His Arg Leu Arg Gln Ile Gln Glu Arg Leu His

145

Thr Ala Ala Leu Pro Ala

150

175

<210> 145 <211> 135 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -25..-1

<400> 145 Met Ser Leu Arg Asn Leu Trp Arg Asp Tyr Lys Val Leu Val Val Met -15 Val Pro Leu Val Gly Leu Ile His Leu Gly Trp Tyr Arg Ile Lys Ser - 5 Ser Pro Val Phe Gln Ile Pro Lys Asn Asp Asp Ile Pro Glu Gln Asp - 10 15 Ser Leu Gly Leu Ser Asn Leu Gln Lys Ser Gln Ile Gln Gly Lys Xaa Ala Gly Leu Gln Ser Ser Gly Lys Glu Ala Ala Leu Asn Leu Ser Phe 45 Ile Ser Lys Glu Glu Met Lys Asn Thr Ser Trp Ile Arg Lys Asn Trp Leu Leu Val Ala Gly Ile Ser Phe Ile Gly Asp His Leu Gly Thr Tyr 80 Phe Leu Gln Arg Ser Ala Lys Gln Ser Val Lys Phe Gln Ser Gln Ser 95 Lys Gln Lys Ser Ile Glu Glu 105

<210> 146 <211> 255 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -70..-1

<400> 146 Met Gln Gln Lys Glu Gln Gln Phe Arg Glu Trp Phe Leu Lys Glu Phe -60 Pro Gln Ile Arg Trp Lys Ile Gln Glu Ser Ile Glu Arg Leu Arg Val -50 Ile Ala Asn Glu Ile Glu Lys Val His Arg Gly Cys Val Ile Ala Asn -30 Val Val Ser Gly Ser Thr Gly Ile Leu Ser Val Ile Gly Val Met Leu -15 -10 Ala Pro Phe Thr Ala Gly Leu Ser Leu Ser Ile Thr Ala Ala Gly Val 1 Gly Leu Gly Ile Ala Ser Ala Thr Ala Gly Ile Ala Ser Ser Ile Val 20 Glu Asn Thr Tyr Thr Arg Ser Ala Glu Leu Thr Ala Ser Arg Leu Thr 35 Ala Thr Ser Thr Asp Gln Leu Glu Ala Leu Arg Asp Ile Leu His Asp 50 . Ile Thr Pro Asn Val Leu Ser Phe Ala Leu Asp Phe Asp Glu Ala Thr WO 99/31236

65 Lys Met Ile Ala Asn Asp Val His Thr Leu Arg Arg Ser Lys Ala Thr 85 80 Val Gly Arg Pro Leu Ile Ala Trp Arg Tyr Val Pro Ile Asn Val Val 100 Glu Thr Leu Arg Thr Arg Gly Ala Pro Thr Arg Ile Val Arg Lys Val 115 110 Ala Arg Asn Leu Gly Lys Ala Thr Ser Gly Val Leu Val Val Leu Asp 130 Val Val Asn Leu Val Gln Asp Ser Leu Asp Leu His Lys Gly Glu Lys . 150 145 Ser Glu Ser Ala Glu Leu Leu Arg Gln Trp Ala Gln Glu Leu Glu Glu 165 160 Asn Leu Asn Glu Leu Thr His Ile His Gln Ser Leu Lys Ala Gly 175

<210> 147 <211> 59 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -49..-1

<400> 147 Met Pro Gly Thr Glu Val Leu Glu Gly Ala Thr Asp Gly Leu Ala Ala -40 -45 Ile Asn Leu Leu Lys Trp Ile Lys Thr Leu Gly Gly Ser Val Ile Ser -25 Met Ile Val Leu Leu Ile Cys Val Val Cys Leu Tyr Ile Val Cys Arg -10 Cys Gly Ser His Leu Trp Arg Glu Ser His His . 5

<210> 148 <211> 180 <212> PRT <213> Homo sapiens

<400> 148 Met Cys Ile Ser Gly Leu Cys Gln Ile Val Gly Cys Asp His Gln Leu Gly Ser Thr Val Lys Glu Asp Asn Cys Gly Val Cys Asn Gly Asp Gly Ser Thr Cys Arg Leu Val Arg Gly Gln Tyr Lys Ser Gln Leu Ser Ala 40 Thr Lys Ser Asp Asp Thr Val Val Ala Ile Pro Tyr Gly Ser Arg His 60 Ile Arg Leu Val Leu Lys Gly Pro Asp His Leu Tyr Leu Glu Thr Lys Thr Leu Gln Gly Thr Lys Gly Glu Asn Ser Leu Ser Ser Thr Gly Thr 90 Phe Leu Val Asp Asn Ser Ser Val Asp Phe Gln Lys Phe Pro Asp Lys 105 Glu Ile Leu Arg Met Ala Gly Pro Leu Thr Ala Asp Phe Ile Val Lys 120 Ile Arg Asn Ser Gly Ser Ala Asp Ser Thr Val Gln Phe Ile Phe Tyr

```
135
                                          140
Gln Pro Ile Ile His Arg Trp Arg Glu Thr Asp Phe Phe Pro Cys Ser
                                   155 • 160
             150
Ala Thr Cys Gly Gly Gly Tyr Gln Leu Thr Ser Ala Glu Cys Tyr Asp
                           170
Leu Arg Ser Asn
           180
<210> 149
<211> 162
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 149
Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala
          -20
                               -15
Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu
Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe
                   15
Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val
Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu
                               50
Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr
                                              70
                          65
Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe
                      80
                                        · 85
Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Pro Asp Asn
                   95
Met Gly Glu Gln Ala Gln Glu Glu Asp Trp Lys Lys Tyr Ile Thr
               110
                                   115
Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Val Ser Met
                               130
Val Phe
<210> 150
<211> 120
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 150
Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala
           -20
                               -15
Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu
                           1
Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe
```

15

20

Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val

Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu 50 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr Cys Ile Arg Ser Lys Asn Gly Pro Gly Thr Ala Val His Ala Tyr Asn 80 Pro Ser Thr Phe Arg Gly Gln Val

<210> 151 <211> 7 <212> PRT . <213> Homo sapiens <400> 151 Met Val Glu Met Thr Gly Val

WO 99/31236

<210> 152 <211> 199 <212> PRT <213> Homo sapiens

<220> <221> SIGNAL <222> -42..-1

<400> 152 Met Asp Gly Gln Lys Lys Asn Trp Lys Asp Lys Val Val Asp Leu Leu -35 -30 Tyr Trp Arg Asp Ile Lys Lys Thr Gly Val Val Phe Gly Ala Ser Leu -20 Phe Leu Leu Ser Leu Thr Val Phe Ser Ile Val Ser Val Thr Ala -5 1 Tyr Ile Ala Leu Ala Leu Leu Ser Val Thr Ile Ser Phe Arg Ile Tyr 15 10 Lys Gly Val Ile Gln Ala Ile Gln Lys Ser Asp Glu Gly His Pro Phe 30 Arg Ala Tyr Leu Glu Ser Glu Val Ala Ile Ser Glu Glu Leu Val Gln 45

Lys Tyr Ser Asn Ser Ala Leu Gly His Val Asn Cys Thr Ile Lys Glu 65 60 Leu Arg Arg Leu Phe Leu Val Asp Asp Leu Val Asp Ser Leu Lys Phe 80 75 Ala Val Leu Met Trp Val Phe Thr Tyr Val Gly Ala Leu Phe Asn Gly 95 Leu Thr Leu Leu Ile Leu Ala Leu Ile Ser Leu Phe Ser Val Pro Val 110 105

Ile Tyr Glu Arg His Gln Ala Gln Ile Asp His Tyr Leu Val Leu Ala

130 125 Asn Lys Asn Val Lys Asp Ala Met Ala Lys Ile Gln Ala Lys Ile Pro 145

Gly Leu Lys Arg Lys Ala Glu

155

<400> 153

 Met
 Pro
 Phe
 Arg
 Met
 Ser Gly
 Tyr
 Ile
 Pro
 Phe
 Gly
 Tyr
 Ile
 Phe
 Ile
 Val

 Ser
 Val
 Thr
 Phe
 Lys
 Gly
 Phe
 Phe
 Phe
 Leu
 Lys
 Asn
 Tyr
 Phe
 Lys
 Cys

 Leu
 Thr
 Leu
 Cys
 Tyr
 Cys
 Ser
 Arg
 Val
 Phe
 Asp

 35
 40
 40

<210> 154 <211> 50 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -37..-1

<400> 154

Met Glu Trp Ala Gly Lys Gln Arg Asp Phe Gln Val Arg Ala Ala Pro
-35
-30
-25
Gly Trp Asp His Leu Ala Ser Phe Pro Gly Pro Ser Leu Arg Leu Phe
-20
-15
-10
Ser Gly Ser Gln Ala Ser Val Cys Ser Leu Cys Ser Gly Phe Gly Ala
-5
1
Gln Glu

<210> 155 <211> 153 <212> PRT <213> Homo sapiens

<400> 155 Thr Val Pro Leu Leu Glu Pro Ala Asp His Ala Arg Gly Arg Ala His Val His Leu Pro Glu Asn Val Arg Ser Gln Ser Pro Gly His Val 25 Arg Arg Gly Arg Ser Gly Ala Gln Val Leu Pro Thr Gly Pro Asp Glu 40 Lys Gln Val Glu Lys Ser Glu Val Asp Phe Ser Lys Ser His Ser Leu 55 Val Arg Arg Phe Glu Asp Leu Lys Pro Lys Leu Ser Val Cys Lys Thr 70 75 Gly Ser Gln Val Phe Arg Ser Glu Asn Trp Lys Val Trp Ala Glu Ser 90 Ser Arg Gly Asp His Asp Asp Cys Leu Asp Leu Cys Ser Val Leu Cys 105 Trp Gly Glu Leu Leu Arg Thr Ile Pro Glu Ile Pro Pro Lys Arg Gly 120 Glu Leu Lys Thr Glu Leu Leu Gly Leu Lys Glu Arg Lys His Lys Pro 135 Gln Val Ser Gln Gln Glu Glu Leu Lys 150

<210> 157 <211> 87 <212> PRT <213> Homo sapiens

11

<210> 158
<211> 250
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -85..-1

-5 Leu Arg Asn Val Arg Gln Leu Glu Asp Leu Val Ile Glu Ala Val Tyr 20 Ala Asp Val Leu Arg Gly Ser Leu Asp Gln Arg Asn Gln Arg Leu Glu Val Asp Tyr Ser Ile Gly Arg Asp Ile Gln Arg Gln Asp Leu Ser Ala 50 Ile Ala Arg Thr Leu Gln Glu Trp Cys Val Gly Cys Glu Val Val Leu . 70 Ser Gly Ile Glu Glu Gln Val Ser Arg Ala Asn Gln His Lys Glu Gln 85. Gln Leu Gly Leu Lys Gln Gln Ile Glu Ser Glu Val Ala Asn Leu Lys 100 Lys Thr Ile Lys Val Thr Thr Ala Ala Ala Ala Ala Thr Ser Gln 115 Asp Pro Glu Gln His Leu Thr Glu Leu Arg Glu Pro Ala Pro Gly Thr 135 130 Asn Gln Arg Gln Pro Ser Lys Lys Ala Ser Lys Gly Lys Gly Leu Arg 145 Gly Ser Ala Lys Ile Trp Ser Lys Ser Asn 160

<210> 159 <211> 24 <212> PRT <213> Homo sapiens

Met Pro Thr Asn Cys Ala Ala Ala Gly Cys Ala Thr Thr Tyr Asn Lys

1 5 10 15

His Ile Asn Ile Ser Phe His Arg
20

<210> 160 <211> 228 <212> PRT <213> Homo sapiens

<400> 160 Met Pro Thr Asn Cys Ala Ala Ala Gly Cys Ala Thr Thr Tyr Asn Lys His Ile Asn Ile Ser Phe His Arg Phe Pro Leu Asp Pro Lys Arg Arg 25 Lys Glu Trp Val Arg Leu Val Arg Arg Lys Asn Phe Val Pro Gly Lys 40 His Thr Phe Leu Cys Ser Lys His Phe Glu Ala Ser Cys Phe Asp Leu Thr Gly Gln Thr Arg Arg Leu Lys Met Asp Ala Val Pro Thr Ile Phe 70 75 Asp Phe Cys Thr His Ile Lys Ser Met Lys Leu Lys Ser Arg Asn Leu 90 Leu Lys Lys Asn Asn Ser Cys Ser Pro Ala Gly Pro Ser Ser Leu Lys 105 Ser Asn Ile Ser Ser Gln Gln Val Leu Leu Glu His Ser Tyr Ala Phe 120 Arg Asn Pro Met Glu Ala Lys Lys Arg Ile Ile Lys Leu Glu Lys Glu 135 Ile Ala Ser Leu Arg Arg Lys Met Lys Thr Cys Leu Gln Lys Glu Arg

150 145 Arg Ala Thr Arg Arg Trp Ile Lys Ala Met Cys Leu Val Lys Asn Leu 170 165 Glu Ala Asn Ser Val Leu Pro Lys Gly Thr Ser Glu His Met Leu Pro 185 180 Thr Ala Leu Ser Ser Leu Pro Leu Glu Asp Phe Lys Ile Leu Glu Gln 195 200 205 Asp Gln Gln Asp Lys Thr Leu Leu Ser Leu Asn Leu Lys Gln Thr Lys 215 220 Ser Thr Phe Ile 225

<210> 161 <211> 86 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -20..-1

<210> 162 <211> 44 <212> PRT <213> Homo sapiens

<210> 163
<211> 314
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -58..-1

Met Gln Asn Val Ile Asn Thr Val Lys Gly Lys Ala Leu Glu Val Ala -50 Glu Tyr Leu Thr Pro Val Leu Lys Glu Ser Lys Phe Arg Glu Thr Gly -35 Val Ile Thr Pro Glu Glu Phe Val Ala Ala Gly Asp His Leu Val His -15 -20 His Cys Pro Thr Trp Gln Trp Ala Thr Gly Glu Glu Leu Lys Val Lys - 5 Ala Tyr Leu Pro Thr Gly Lys Gln Phe Leu Val Thr Lys Asn Val Pro Cys Tyr Lys Arg Cys Lys Gln Met Glu Tyr Ser Asp Glu Leu Glu Ala 30 Ile Ile Glu Glu Asp Asp Gly Asp Gly Gly Trp Val Asp Thr Tyr His 45 Asn Thr Gly Ile Thr Gly Ile Thr Glu Ala Val Lys Glu Ile Thr Leu 60 65 Glu Asn Lys Asp Asn Ile Arg Leu Gln Asp Cys Ser Ala Leu Cys Glu 80 75 Glu Glu Glu Asp Glu Asp Glu Gly Glu Ala Ala Asp Met Glu Glu Tyr 95 Glu Glu Ser Gly Leu Leu Glu Thr Asp Glu Ala Thr Leu Asp Thr Arg 110 Lys Ile Val Glu Ala Cys Lys Ala Lys Thr Asp Ala Gly Gly Glu Asp 125 , 130 Ala Ile Leu Gln Thr Arg Thr Tyr Asp Leu Tyr Ile Thr Tyr Asp Lys 140 145 Tyr Tyr Gln Thr Pro Arg Leu Trp Leu Phe Gly Tyr Asp Glu Gln Arg 155 160 Gln Pro Leu Thr Val Glu His Met Tyr Glu Asp Ile Ser Gln Asp His 175 Val Lys Lys Thr Val Thr Ile Glu Asn His Pro His Leu Pro Pro Pro 190 195 Pro Met Cys Ser Val His Pro Cys Arg His Ala Glu Val Met Lys Lys 205 Ile Ile Glu Thr Val Ala Glu Gly Gly Glu Leu Gly Val His Met 225 220 Tyr Leu Leu Ile Phe Leu Lys Phe Val Gln Ala Val Ile Pro Thr Ile 240 235 Glu Tyr Asp Tyr Thr Arg His Phe Thr Met

<210> 164 <211> 89 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -80..-1

-25 Gln Leu Gly Arg Gly Leu Leu Ser Ala Cys Ala Pro Trp Gly Asp Gly -10 Ser Thr Gln Pro Val Pro Leu Cys Ser . 5

<210> 165 <211> 98 <212> PRT <213> Homo sapiens

<220> <221> SIGNAL <222> -15..-1

<400> 165 Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu Ala Val Leu Ala Trp -10 -5 Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg Met Lys Ser Arg Glu Gln Gly Gly Arg Leu Gly Ala Glu Ser Arg Thr Leu Leu Val Ile Ala 25 His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro Thr Val Leu Gly Leu 45 40 Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys Phe Ser Ala Val Phe 55 60 Arg Arg Glu Leu Ser Glu Tyr Thr Glu Gly Leu Thr Ser Glu Pro Leu 75

Thr Ala

<210> 166 <211> 92 <212> PRT <213> Homo sapiens

<220> <221> SIGNAL <222> -36..-1

<400> 166 Met Leu Val Thr Gln Gly Leu Val Tyr Gln Gly Tyr Leu Ala Ala Asn -30 Ser Arg Phe Gly Ser Leu Pro Lys Val Ala Leu Ala Gly Leu Leu Gly -15 -10 Phe Gly Leu Gly Lys Val Ser Tyr Ile Gly Val Cys Gln Ser Lys Phe

His Phe Phe Glu Asp Gln Leu Arg Gly Ala Gly Phe Gly Pro Gln His Asn Arg His Cys Leu Leu Thr Cys Glu Glu Cys Lys Ile Lys His Gly

-25

35 Leu Ser Glu Lys Gly Asp Ser Gln Pro Ser Ala Ser 50

<210> 167 <211> 351 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -16..-1 <400> 167 Met Val Pro Phe Ile Tyr Leu Gln Ala His Phe Thr Leu Cys Ser Gly -10 Trp Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr 40 Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Pro Glu Pro 70 Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser 90 Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu 105 Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu 120 115 125 Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr 135 140 Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met 150 155 Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr 165 170 Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser 185 Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu 200 Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile 215 220 Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser 230 235 Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp 245 250 Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser 265 Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val 280 Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys 295 His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Cys 310 315 His Leu Gly His Gly Arg Leu Trp Leu Gln His Ser Thr Asp Arg

330

<210> 168 <211> 138 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<222> -47..-1

<400> 168 Met Glu Lys Phe Val Asp Pro Gly Asn His Asn Ser Gly Ile Asp Leu -45 -40 Leu Arg Thr Tyr Leu Trp Arg Cys Gln Phe Leu Leu Pro Phe Val Ser -25 -20 Leu Gly Leu Met Cys Phe Gly Ala Leu Ile Gly Leu Cys Ala Cys Ile -10 - 5. Cys Arg Ser Leu Tyr Pro Thr Ile Ala Thr Gly Ile Leu His Leu Leu 10 Ala Gly Leu Cys Thr Leu Gly Ser Val Ser Cys Tyr Val Ala Gly Ile 20 **25** . . Glu Leu Leu His Gln Lys Leu Glu Leu Pro Asp Asn Val Ser Gly Glu Phe Gly Trp Ser Phe Cys Leu Ala Cys Val Ser Ala Pro Leu Gln Phe 55 60 Met Ala Ser Ala Leu Phe Ile Trp Ala Ala His Thr Asn Arg Arg Glu 75 70 Tyr Thr Leu Met Lys Ala Tyr Arg Val Ala

<210> 169 <211> 101 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<222> -73..-1

<400> 169 Met Asn Leu Glu Arg Val Ser Asn Glu Glu Lys Leu Asn Leu Cys Arg -70 -65 Lys Tyr Tyr Leu Gly Gly Phe Ala Phe Leu Pro Phe Leu Trp Leu Val -55 -50 Asn Ile Phe Trp Phe Tyr Arg Glu Ala Phe Leu Val Pro Ala Tyr Thr -35 -30 Glu Gln Ser Gln Ile Lys Gly Tyr Val Trp Arg Ser Ala Val Gly Phe -20 -15 Leu Phe Trp Val Ile Val Leu Thr Ser Trp Ile Thr Ile Phe Gln Ile -5 Tyr Arg Pro Arg Trp Gly Ala Leu Gly Asp Tyr Leu Ser Phe Thr Ile Pro Leu Gly Thr Pro 25

<210> 170 <211> 252 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -68..-1

Ala Cys Arq Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser -30 -25 Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro -15 -10 Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His 20 Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys - 50 55 Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Gln Glu Tyr Gln Gln Phe 70 Arg Glu Asn Val Leu Arg Asn Leu Ala Asp Lys Ala Phe Asp Arg Pro Ile Cys Glu Ala Leu Leu Asp Gln Arg Phe Phe Asn Gly Ile Gly Asn 100 105 Tyr Leu Arg Ala Glu Ile Leu Tyr Arg Leu Lys Ile Pro Pro Phe Glu 115 Lys Ala Arg Ser Val Leu Glu Ala Leu Gln Gln His Arg Pro Ser Pro 130 135 Glu Leu Thr Leu Ser Gln Lys Ile Arg Thr Lys Leu Gln Asn Ser Asp 145 150 Leu Leu Glu Leu Cys His Ser Val Pro Lys Glu Val Val Gln Leu Gly 165 160 Glu Ala Lys Asp Gly Ser Asn Leu Cys Phe Ser Lys

<210> 171 <211> 350 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<400> 171

<222> -68..-1

Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu -60 Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val -45 Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser -30 Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro -15 -10 Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His 20 Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Gln Glu Tyr Gln Gln Phe Arg Leu Lys Ile Pro Pro Phe Glu Lys Ala Arg Ser Val Leu Glu Ala

WO 99/31236 -129- PCT/IB98/02122 -

```
85
Leu Gln Gln His Arg Pro Ser Pro Glu Leu Thr Leu Ser Gln Lys Ile
                          100
Arg Thr Lys Leu Gln Asn Pro Asp Leu Leu Glu Leu Cys His Ser Val
                                          120
                      115
Pro Lys Glu Val Asp Gln Leu Gly Gly Arg Gly Tyr Gly Ser Glu Ser
                                       135
                   130
Gly Glu Glu Asp Phe Ala Ala Phe Arg Ala Trp Leu Arg Cys Tyr Gly
                                   150
               145
Met Pro Gly Met Ser Ser Leu Gln Asp Arg His Gly Arg Thr Ile Trp
                               165
Phe Gln Gly Asp Pro Gly Pro Leu Ala Pro Lys Gly Arg Lys Ser Arg
                           180
Lys Lys Lys Ser Lys Ala Thr Gln Leu Ser Pro Glu Asp Arg Val Glu
                                           200
            195
Asp Ala Leu Pro Pro Ser Lys Ala Pro Ser Lys Thr Arg Arg Ala Lys
                   210
                                       215
Arg Asp Leu Pro Lys Arg Thr Ala Thr Gln Arg Pro Glu Gly Thr Ser
                                  230
               225
Leu Gln Gln Asp Pro Glu Ala Pro Thr Val Pro Lys Lys Gly Arg Arg
                               245
           240
Lys Gly Arg Gln Ala Ala Ser Gly His Cys Arg Pro Arg Lys Val Lys
                        260
Ala Asp Ile Pro Ser Leu Glu Pro Glu Gly Thr Ser Ala Ser
                        275
    270
```

<210> 172 <211> 390

<212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -68..-1 <400> 172 Met Pro Glu Gly Pro Glu Leu His Leu Ala Ser Gln Phe Val Asn Glu -60 Ala Cys Arg Ala Leu Val Phe Gly Gly Cys Val Glu Lys Ser Ser Val -45 Ser Arg Asn Pro Glu Val Pro Phe Glu Ser Ser Ala Tyr Arg Ile Ser -30 Ala Ser Ala Arg Gly Lys Glu Leu Arg Leu Ile Leu Ser Pro Leu Pro -10 -15 Gly Ala Gln Pro Gln Gln Glu Pro Leu Ala Leu Val Phe Arg Phe Gly Met Ser Gly Ser Phe Gln Leu Val Pro Arg Glu Glu Leu Pro Arg His 20 Ala His Leu Arg Phe Tyr Thr Ala Pro Pro Gly Pro Arg Leu Ala Leu 35 Cys Phe Val Asp Ile Arg Arg Phe Gly Arg Trp Asp Leu Gly Gly Lys Trp Gln Pro Gly Arg Gly Pro Cys Val Leu Gln Glu Tyr Gln Gln Phe Arg Glu Asn Val Leu Arg Asn Leu Ala Asp Lys Ala Phe Asp Arg Pro Ile Cys Glu Ala Leu Leu Asp Gln Arg Phe Phe Asn Gly Ile Gly Asn 100 105 Tyr Leu Arg Ala Glu Ile Leu Tyr Arg Leu Lys Ile Pro Pro Phe Glu WO 99/31236 -130 - PCT/IB98/02122 -

Lys Ala Arg Ser Val Leu Glu Ala Leu Gln Gln His Arg Pro Ser Pro 135 130 Glu Leu Thr Leu Ser Gln Lys Ile Arg Thr Lys Leu Gln Asn Pro Asp 150 145 Leu Leu Glu Leu Cys His Ser Val Pro Lys Glu Val Val Gln Leu Gly 165 Gly Arg Gly Tyr Gly Ser Glu Ser Gly Glu Glu Asp Phe Ala Ala Phe 175 180 Arg Ala Trp Leu Arg Cys Tyr Gly Met Pro Gly Met Ser Ser Leu Gln 195 Asp Arg His Gly Arg Thr Ile Trp Phe Gln Gly Asp Pro Gly Pro Leu 205 210 Ala Pro Lys Gly Arg Lys Ser Arg Lys Lys Ser Lys Ala Thr Gln . 230 225 Leu Ser Pro Glu Asp Arg Val Glu Asp Ala Leu Pro Pro Ser Lys Ala Pro Ser Arg Thr Arg Arg Ala Lys Arg Asp Leu Pro Lys Arg Thr Ala 260 Thr Gln Arg Pro Glu Gly Thr Ser Leu Gln Gln Asp Pro Glu Ala Pro 275 Thr Val Pro Lys Lys Gly Arg Arg Lys Gly Arg Gln Ala Ala Ser Gly 290 295 His Cys Arg Pro Arg Lys Val Lys Ala Asp Ile Pro Ser Leu Glu Pro 305 310 Glu Gly Thr Ser Ala Ser 320

<210> 173 <211> 190 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -82..-1

<400> 173

Met Tyr Val Trp Pro Cys Ala Val Val Leu Ala Gln Tyr Leu Trp Phe -75 His Arg Arg Ser Leu Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala Gly -60 Val Ser Leu Pro Gly Ile Leu Thr Ala Lys Cys Gly Ala Glu Val Ile -45 Leu Ser Asp Ser Ser Glu Leu Pro His Cys Leu Glu Val Cys Arg Gln -25 -30 Ser Cys Gln Met Asn Asn Leu Pro His Leu Gln Val Val Gly Leu Thr -10 -15 Trp Gly His Ile Ser Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp Ile 10 Ile Leu Ala Ser Asp Val Phe Phe Glu Pro Glu Asp Phe Glu Asp Ile 20 Leu Ala Thr Ile Tyr Phe Leu Met His Lys Asn Pro Lys Val Gln Leu Trp Ser Thr Tyr Gln Val Arg Ser Ala Asp Trp Ser Leu Glu Ala Leu Leu Tyr Lys Trp Asp Met Lys Cys Val His Ile Pro Leu Glu Ser Phe 70 Asp Ala Asp Lys Glu Asp Ile Ala Glu Ser Thr Leu Pro Gly Arg His

Thr Val Glu Met Leu Val Ile Ser Phe Ala Lys Asp Ser Leu

105

-30

20

-15

95 ( 100

<210> 174 <211> 285 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -232..-1 <400> 174 Met Gly Cys Val Phe Gln Ser Thr Glu Asp Lys Arg Ile Phe Lys Ile -230 -225 -220 Asp Trp Thr Leu Ser Pro Gly Glu His Ala Lys Asp Glu Tyr Val Leu -210 -205 Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg -195 -190 -200 Val His Leu Met Gly Asp Asn Leu Cys Asn Asp Gly Ser Leu Leu Leu -180 -175 Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg -165 -160 Leu Lys Gly Glu Ser Gln Val Phe Lys Lys Ala Val Val Leu His Val -145 -140 -150 Leu Pro Glu Glu Pro Lys Glu Leu Met Val His Val Gly Gly Leu Ile -130 -125 Gln Met Gly Cys Val Phe Gln Ser Thr Glu Val Lys His Val Thr Lys -115 -110 Val Glu Trp Ile Phe Ser Gly Arg Arg Ala Lys Glu Glu Ile Val Phe - 95 Arg Tyr Tyr His Lys Leu Arg Met Ser Ala Glu Tyr Ser Gln Ser Trp -80 -75 Gly His Phe Gln Asn Arg Val Asn Leu Val Gly Asp Ile Phe Arg Asn -70 -65 Asp Gly Ser Ile Met Leu Gln Gly Val Arg Glu Ser Asp Gly Gly Asn -50 Tyr Thr Cys Ser Ile His Leu Gly Asn Leu Val Phe Lys Lys Thr Ile

Val Leu His Val Ser Pro Glu Glu Pro Arg Thr Leu Val Thr Pro Ala

Ala Leu Arg Pro Leu Val Leu Gly Gly Asn Gln Leu Val Ile Ile Val

Gly Ile Val Cys Ala Thr Ile Leu Leu Leu Pro Val Leu Ile Leu Ile

Val Lys Lys Thr Cys Gly Asn Lys Ser Ser Val Asn Ser Thr Val Leu

<210> 175 <211> 153 <212> PRT

-35

30

15

Val Lys Asn Thr Lys Lys Thr Asn Pro Lys Lys Lys

-20

45

<213> Homo sapiens

WO 99/31236 -132- PCT/IB98/02122 -

Tyr Tyr Tyr Ser Asn Leu Ser Val Pro Ile Gly Arg Phe Gln Asn Arg 40 Val His Leu Met Gly Asp Ile Leu Cys Asn Asp Gly Ser Leu Leu Leu 55 Gln Asp Val Gln Glu Ala Asp Gln Gly Thr Tyr Ile Cys Glu Ile Arg 70 75 Leu Lys Gly Glu Ser Gln Val Phe Lys Lys Ala Val Val Leu His Val ·85 90 Leu Pro Glu Glu Pro Lys Glu Leu Met Val His Val Gly Gly Leu Ile 110 105 Gln Met Gly Cys Val Phe Gln Ser Thr Glu Val Lys His Val Thr Lys 120 Val Glu Trp Ile Phe Ser Gly Arg Arg Ala Lys Val Thr Arg Arg Lys 135 His His Cys Val Arg Glu Gly Ser Gly 150

<210> 176 <211> 49 <212> PRT <213> Homo sapiens

<400> 176

 Met
 Leu
 Xaa
 Gly
 Asp
 His
 Arg
 Ala
 Leu
 Leu
 Leu
 Lys
 Ile
 Trp
 Leu
 Leu

 1
 5
 10
 15
 15

 Gln
 Arg
 Pro
 Glu
 Ser
 Gln
 Glu
 Gly
 Leu
 Pro
 Gly
 Arg
 Leu
 Val
 Val

<210> 177
<211> 99
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1

75

<400> 177

 Met
 Lys
 Ser
 Ala
 Lys
 Leu
 Gly
 Phe
 Leu
 Leu
 Arg
 Phe
 Phe
 Phe
 Phe
 Cys

 Ser
 Leu
 Asn
 Thr
 Leu
 Leu
 Leu
 Gly
 Val
 Asn
 Lys
 Ile
 Ala
 Glu
 Lys

 Ile
 Cys
 Gly
 Asp
 Leu
 Lys
 Asp
 Pro
 Cys
 Lys
 Leu
 Asp
 Met
 Asn
 Phe
 Gly
 Ile
 Asn
 Phe
 Gly
 Ile
 Asn
 Asn
 Phe
 Ile
 Asn
 Asn
 Phe
 Ile
 Asn
 Asn

```
<210> 178
<211> 95
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -37..-1
<400> 178
Met Ala Ser Pro Ala Val Asn Arg Trp Lys Arg Pro Arg Leu Lys Pro
                            -30
Val Trp Pro Arg Arg Leu Glu Ser Trp Leu Leu Leu Asp Ala Leu Leu
                                            -10
                        -15
Arg Leu Gly Asp Thr Lys Lys Lys Arg Gln Pro Glu Ala Ala Thr Lys
                    1
Ser Cys Val Arg Ser Ser Cys Gly Gly Pro Ser Gly Asp Gly Pro Pro
                                20
Pro Cys Leu Gln Gln Pro Asp Pro Arg Ala Leu Ser Gln Ala Phe Ser
       30
                            35
Arg Ser Phe Pro Leu Phe Pro Ser Leu Ala Gly Lys Ser Met Ile
    45
<210> 179
<211> 121
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -23..-1
 <400> 179
 Met Met Leu Pro Gln Trp Leu Leu Leu Phe Leu Leu Phe Phe Phe
                                 -15
            -20
 Leu Phe Leu Leu Thr Arg Gly Ser Leu Ser Pro Thr Lys Tyr Asn Leu
 Leu Glu Leu Lys Glu Ser Cys Ile Arg Asn Gln Asp Cys Glu Thr Gly
                     15
 Cys Cys Gln Arg Ala Pro Asp Asn Cys Glu Ser His Cys Ala Glu Lys
                                     35
 Gly Ser Glu Gly Ser Leu Cys Gln Thr Gln Val Phe Phe Gly Gln Tyr
                                 50
 Arg Ala Cys Pro Cys Leu Arg Asn Leu Thr Cys Ile Tyr Ser Lys Asn
                             65
 Glu Lys Trp Leu Ser Ile Ala Tyr Gly Arg Cys Gln Lys Ile Gly Arg
                         80
 Gln Lys Leu Ala Lys Lys Met Phe Phe
  <210> 180
```

<211> 59 <212> PRT <213> Homo sapiens

<400> 180 Met Ile Leu Cys Phe Leu Leu Pro His His Arg Leu Gln Glu Ala Arg

<210> 181 <211> 86 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -14..-1

<400> 181

Met Val Ala Leu Asn Leu Ile Leu Val Pro Cys Cys Ala Ala Trp Cys
-10 -5 1

Asp Pro Arg Arg Ile His Ser Gln Asp Asp Val Pro Arg Ser Ser Ala
5 10 15

Ala Asp Thr Gly Ser Ala Met Gln Arg Arg Glu Ala Trp Ala Gly Trp
20 25 30

Arg Arg Ser Gln Pro Phe Ser Val Gly Leu Pro Ser Ala Glu Arg Leu
35 40 45 50

Glu Asn Gln Pro Gly Lys Leu Ser Trp Arg Ser Leu Val Gly Glu Gly
55 60 65

Tyr Arg Ile Cys Asp Leu 70

<210> 182 <211> 165 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -58..-1

Lys Leu Leu Thr Arg Gly Gln Ser Gln Gly Ala Gly Glu Gly Pro Gly
40 45 50

Gln Gln Glu Ala Leu Leu Leu Gln Met Gly Thr Val Ser Gly Gln Leu
55 60 65 70

Ser Leu Gln Asp Ala Leu Leu Leu Leu Leu Met Gly Leu Gly Pro Leu

Leu Arg Ala Cys Gly Met Pro Leu Thr Leu Leu Gly Leu Ala Phe Cys 90 95 100

Leu His Pro Trp Ala 105

<210> 183
<211> 80
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -35..-1

<400> 183
Met Pro Phe Gln Phe Gly Thr Gln Pro Arg Arg Phe Pro Val Glu Gly
-35
-30
-25
-20

Thr Thr Arg Lys Pro Pro Ala Gln Ser Ser Lys Glu Met His Pro Lys 30 35 40 45

<210> 184 <211> 73 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -21. -1

1.1

<210> 185 <211> 98 <212> PRT <213> Homo sapiens

<400> 185
Met Leu Gly Ala Glu Thr Glu Glu Lys Leu Phe Asp Ala Pro Leu Ser
1 5 10 15

 Ile
 Ser
 Lys
 Arg
 Glu
 Gln
 Leu
 Glu
 Gln
 Gln
 Gln
 Gln
 Gln
 Val
 Pro
 Glu
 Asn
 Tyr
 Phe
 30
 Tyr
 Phe
 30
 Tyr
 Asn
 Tyr
 Ser
 Tyr
 Asn
 Tyr
 Glu
 Pro
 Ser
 Tyr
 Tyr
 Asn
 Asn
 Asn
 Asn
 Leu
 Met
 Tyr
 Ile
 Ala
 Asn
 Asn

<210> 186 <211> 112 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -21..-1

<210> 187 <211> 70 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -44..-1 <400> 187

 Addos 187

 Met Cys Cys Tyr Cys Arg Ile Phe Cys Leu Arg Cys Thr Tyr Phe Pro -40
 -35
 -30

 Val His Cys Gly Met Cys Asn Leu Arg Tyr Phe Glu Phe Ser Thr Phe -25
 -15

 Leu Leu Ser Leu Ser Leu Ile Thr Tyr Cys Phe Trp Asp Pro Pro His -10
 -5
 1

 Arg Gly Ser His Ser Leu Ser Leu Glu His Thr Pro Leu Asp Phe Leu 10
 15
 20

 Glu Trp Gly Leu Leu Arg 25
 25
 20

```
<210> 188
 <211> 92
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -13..-1
 <400> 188
Met Leu Phe Ser Leu Ser Leu Ser Asn Leu Asn Gln Ile Gly Ser
        -10
                                -5
Ser His Leu Asp Arg Pro His Ile Pro Gly Gln Ser Ala Gln Leu Phe
 Ile Tyr Gln Met Ser Ser Gln Gln Leu Gln Gln Gln Pro Ser Ala Asn
                                         30
 Lys Lys Ala Gly Lys Ile His Asn Thr Pro Phe Ala Asn Gln Leu Asn
                                     45
                 40
 Pro Thr Gln His Leu Ala Lys Pro Phe Gln Gln Ile Leu Pro Gly Arg
                                 60
 Gln Ser Gly Ser Leu Thr Ser Pro Phe Leu Ala Cys
                             75
 <210> 189
 <211> 207
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -42..-1
 <400> 189
 Met His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala
                             -35
  Ile Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe
                          -20
                                             -15
  Asp Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Pro Ile Ile
                     -5
  Leu Gln Glu Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser
                                  15
  Ala Ile Tyr Ala Ser Gln Thr Glu Gln Glu Tyr Leu Lys Ile Glu Lys
                             30
  Val Asp Leu Pro Leu Ile Asp Ser Leu Ile Arg Val Leu Gln Asn Met
                          45
  Glu Gln Cys Gln Lys Lys Pro Glu Asn Ser Ala Glu Ser Asn Thr Glu
                                          65
                      60
  Glu Thr Lys Arg Thr Asp Leu Thr Gln Asp Asp Leu His Leu Lys Ile
                                      80
```

Leu Lys Asp Ile Leu Cys Glu Phe Leu Ser Asn Ile Phe Gln Ala Leu

Thr Lys Glu Thr Val Ala Gln Gly Val Lys Glu Gly Gln Leu Ser Lys 110

Gln Lys Cys Ser Ser Ala Phe Gln Asn Leu Leu Pro Phe Tyr Ser Pro

Val Val Glu Asp Phe Ile Lys Ile Leu Arg Glu Val Asp Lys Ala Leu

Ala Asp Asp Leu Glu Lys Asn Phe Pro Ser Leu Lys Val Gln Thr

125

140

115

130

<210> 190

155

160

165

```
<211> 201
<212> PRT
<213> Homo sapiens
<400> 190 · ·
Met Gln Val Ala Leu Lys Glu Asp Leu Asp Ala Leu Lys Glu Lys Phe
                                    .10
Arg Thr Met Glu Ser Asn Gln Lys Ser Ser Phe Gln Glu Ile Pro Lys
Leu Asn Glu Glu Leu Leu Ser Lys Gln Lys Gln Leu Glu Lys Ile Glu
Ser Gly Glu Met Gly Leu Asn Lys Val Trp Ile Asn Ile Thr Glu Met
Asn Lys Gln Ile Ser Leu Leu Thr Ser Ala Val Asn His Leu Lys Ala
                                       · 75
Asn Val Lys Ser Ala Ala Asp Leu Ile Ser Leu Pro Thr Thr Val Glu
                                    90
Gly Leu Gln Lys Ser Val Ala Ser Ile Gly Asn Thr Leu Asn Ser Val
                                105
His Leu Ala Val Glu Ala Leu Gln Lys Thr Val Asp Glu His Lys Lys
                            120
Thr Met Glu Leu Leu Gln Ser Asp Met Asn Gln His Phe Leu Lys Glu
                        135
                                            140
Thr Pro Gly Ser Asn Gln Ile Ile Pro Ser Pro Ser Ala Thr Ser Glu
                    150
                                         155
Leu Asp Asn Lys Thr His Ser Glu Asn Leu Lys Gln Met Gly Asp Arg
                165
                                    170
Ser Ala Thr Leu Lys Arg Gln Ser Leu Asp Gln Val Thr Asn Arg Thr
                                185
Asp Thr Val Lys Ile Gln Lys Lys
        195
                             200
```

<210> 191

<211> 379

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -37..-1

<400> 191

Met Pro His Ser Ser Leu His Pro Ser Ile Pro Cys Pro Arg Gly His
-35 -30 -25

Gly Ala Gln Lys Ala Ala Leu Val Leu Leu Ser Ala Cys Leu Val Thr
-20 -15 -10

Leu Trp Gly Leu Gly Glu Pro Pro Glu His Thr Leu Arg Tyr Leu Val
-5 1 5 10

Leu His Leu Ala Ser Leu Gln Leu Gly Leu Leu Leu Asn Gly Val Cys
15 20 25

Ser Leu Ala Glu Glu Leu Arg His Ile His Ser Arg Tyr Arg Gly Ser 30 35 40

Tyr Trp Arg Thr Val Arg Ala Cys Leu Gly Cys Pro Leu Arg Arg Gly
45 50 55

Ala Leu Leu Leu Leu Ser Ile Tyr Phe Tyr Tyr Ser Leu Pro Asn Ala

```
65
                                      70
Val Gly Pro Pro Phe Thr Trp Met Leu Ala Leu Leu Gly Leu Ser Gln
               80
                                 85
Ala Leu Asn Ile Leu Leu Gly Leu Lys Gly Leu Ala Pro Ala Glu Ile
                              100
Ser Ala Val Cys Glu Lys Gly Asn Phe Asn Val Ala His Gly Leu Ala
                          115
Trp Ser Tyr Tyr Ile Gly Tyr Leu Arg Leu Ile Leu Pro Glu Leu Gln
                                         135
                      130
Ala Arg Ile Arg Thr Tyr Asn Gln His Tyr Asn Asn Leu Leu Arg Gly
     145 150
Ala Val Ser Gln Arg Leu Tyr Ile Leu Leu Pro Leu Asp Cys Gly Val
         160
                                 165
Pro Asp Asn Leu Ser Met Ala Asp Pro Asn Ile Arg Phe Leu Asp Lys
                              180
           175
Leu Pro Gln Gln Thr Gly Asp Arg Ala Gly Ile Lys Asp Arg Val Tyr
                           195
Ser Asn Ser Ile Tyr Glu Leu Leu Glu Asn Gly Gln Arg Ala Gly Thr
                       210
Cys Val Leu Glu Tyr Ala Thr Pro Leu Gln Thr Leu Phe Ala Met Ser
                  225
                                     1230
Gln Tyr Ser Gln Ala Gly Phe Ser Arg Glu Asp Arg Leu Glu Gln Ala
                                 245
Lys Leu Phe Cys Arg Thr Leu Glu Asp Ile Leu Ala Asp Ala Pro Glu
                              260
           255
Ser Gln Asn Asn Cys Arg Leu Ile Ala Tyr Gln Glu Pro Ala Asp Asp
                          275
Ser Ser Phe Ser Leu Ser Gln Glu Val Leu Arg His Leu Arg Gln Glu
                       290
                                          295
Glu Lys Glu Glu Val Thr Val Gly Ser Leu Lys Thr Ser Ala Val Pro
               305
                                     310
Ser Thr Ser Thr Met Ser Gln Glu Pro Glu Leu Leu Ser Gly Met
               320
                                  325
Gly Lys Pro Leu Pro Leu Arg Thr Asp Phe Ser
                               340
```

<210> 192 <211> 112 <212> PRT <213> Homo sapiens

<400> 192

 Met
 Pro
 Ser
 Glu
 Gly
 Arg
 Cys
 Trp
 Glu
 Thr
 Leu
 Lys
 Ala
 Leu
 Arg
 Ser

 Ser
 Asp
 Lys
 Gly
 Arg
 Leu
 Cys
 Tyr
 Tyr
 Arg
 Asp
 Trp
 Leu
 Leu
 Arg
 Arg
 Asp
 Trp
 Leu
 Leu
 Arg
 Arg
 Asp
 Trp
 Leu
 Leu
 Arg
 Arg

<400> 193

 Ser Leu Pro Gln Ala Leu Trp Phe Gln Phe Phe Tyr His Ser Gly Ser

 1
 5
 10
 15

 Ser Leu Glu Ser Pro Gly Met Leu Asn Gly Pro Phe Gln His Arg Asn 20
 25
 30

 Ser Arg Ile Met Thr His Arg Ser Ala Glu Lys 35
 40

<210> 194 <211> 51 <212> PRT <213> Homo sapiens <220>

<400> 194

<221> SIGNAL <222> -16..-1

Met Leu Arg Ile Ala Leu Thr Leu Ile Pro Ser Met Leu Ser Arg Ala
-15
-10
-5

Ala Gly Trp Cys Trp Tyr Lys Glu Pro Thr Gln Gln Phe Ser Tyr Leu
1
5
Cys Leu Pro Cys Leu Ser Trp Asn Lys Lys Gly Asn Val Leu Gln Leu
20
25
30

Pro Asn Phe

Pro Asn Phe 35

<210> 195
<211> 244
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -18..-1

Phe Arg Ile Pro Met Ser Leu Gly Glu Pro His Ala Glu Leu Asp Ala 80 85 90 Lys Gly Gln Gly Cys Thr Ala Tyr Asp Val Ala Val Asn Ser Asp Phe 95 100 105 110

Tyr Arg Arg Met Gln Asn Ser Asp Phe Leu Arg Glu Leu Val Ile Thr

120 115 Ile Ala Arg Glu Gly Leu Glu Asp Ile Tyr Asn Leu Gln Leu Asn Pro 130 135 140 Glu Trp Arg Met Met Lys Asn Arg Pro Phe Met Gly Ser Ile Ser Gln 150 Gln Asn Ile Arg Ser Glu Gln Arg Pro Arg Ile Gln Glu Leu Gly Asp 165 170 Leu Tyr Thr Pro Ala Pro Gly Arg Ala Glu Ser Gly Pro Glu Lys Pro 185 180 His Leu Asn Leu Trp Leu Glu Ala Pro Asp Leu Leu Leu Ala Glu Val 195 200 Asp Leu Pro Lys Leu Asp Gly Ala Leu Gly Leu Ser Leu Glu Ile Gly 215 Arg Thr Ala Trp 225

<210> 196 <211> 353 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -34..-1

<222> -34.

<400> 196 Met Glu Arg Gly Leu Lys Ser Ala Asp Pro Arg Asp Gly Thr Gly Tyr -25 -30 Thr Gly Trp Ala Gly Ile Ala Val Leu Tyr Leu His Leu Tyr Asp Val -15 -10 Phe Gly Asp Pro Ala Tyr Leu Gln Leu Ala His Gly Tyr Val Lys Gln Ser Leu Asn Cys Leu Thr Lys Arg Ser Ile Thr Phe Leu Cys Gly Asp 20 Ala Gly Pro Leu Ala Val Ala Ala Val Leu Tyr His Lys Met Asn Asn 40 Glu Lys Gln Ala Glu Asp Cys Ile Thr Arg Leu Ile His Leu Asn Lys 55 Ile Asp Pro His Ala Pro Asn Glu Met Leu Tyr Gly Arg Ile Gly Tyr 70 Ile Tyr Ala Leu Leu Phe Val Asn Lys Asn Phe Gly Val Glu Lys Thr 85 Pro Gln Ser His Ile Gln Gln Ile Cys Glu Thr Ile Leu Thr Ser Gly 105 100 Glu Asn Leu Ala Arg Lys Arg Asn Phe Thr Ala Lys Ser Pro Leu Met 120 115 Tyr Glu Trp Tyr Gln Glu Tyr Tyr Val Gly Ala Ala His Gly Leu Ala 135 130 Gly Ile Tyr Tyr Leu Met Gln Pro Ser Leu Gln Val Ser Gln Gly 150 Lys Leu His Ser Leu Val Lys Pro Ser Val Asp Tyr Val Cys Gln Leu 165 170 Lys Phe Pro Ser Gly Asn Tyr Pro Pro Cys Ile Gly Asp Asn Arg Asp 180 185 Leu Leu Val His Trp Cys His Gly Ala Pro Gly Val Ile Tyr Met Leu 195 200 Ile Gln Ala Tyr Lys Val Phe Arg Glu Glu Lys Tyr Leu Cys Asp Ala 215 Tyr Gln Cys Ala Asp Val Ile Trp Gln Tyr Gly Leu Leu Lys Lys Gly 230

<210> 197 <211> 30 <212> PRT <213> Homo sapiens

<210> 198 <211> 112 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -48..-1

<400> 198 Met Gln Asp Thr Gly Ser Val Val Pro Leu His Trp Phe Gly Phe Gly -35 -45 -40 Tyr Ala Ala Leu Val Ala Ser Gly Gly Ile Ile Gly Tyr Val Lys Ala -25 -20 -30 Gly Ser Val Pro Ser Leu Ala Ala Gly Leu Leu Phe Gly Ser Leu Ala -10 Gly Leu Gly Ala Tyr Gln Leu Ser Gln Asp Pro Arg Asn Val Trp Val Phe Leu Ala Thr Ser Gly Thr Leu Ala Gly Ile Met Gly Met Arg Phe Tyr His Ser Gly Lys Phe Met Pro Ala Gly Leu Ile Ala Gly Ala Ser Leu Leu Met Val Ala Lys Val Gly Val Ser Met Phe Asn Arg Pro His 55

<210> 199 <211> 54 <212> PRT <213> Homo sapiens

<400> 199
Glu Ile Ala Gly Tyr Gly Ala Glu Gly Phe Ser Ser Val Leu Gly Tyr
1 5 10 15

<210> 200

 Pro Arg Trp
 His Arg
 Leu Pro Pro Gln Ser Leu Gln His His Gln Tyr

 20
 25
 30

 Cys Gln Arg Arg Trp Pro Asp Arg Arg Cys Leu Gln Ser His Thr Gln
 35
 40

 Ser Ser Gly His Leu Pro
 50

<211> 151 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -21..-1 <400> 200 Met Ala Ala Ser Thr Ser Met Xaa Pro Val Ala Val Thr Ala Ala Val -10 -15 Ala Pro Val Leu Ser Ile Asn Ser Asp Phe Ser Asp Leu Arg Glu Ile 5 1 Lys Lys Gln Leu Leu Leu Ile Ala Gly Leu Thr Arg Glu Arg Gly Leu 20 Leu His Ser Ser Lys Trp Ser Ala Glu Leu Ala Phe Ser Leu Pro Ala 40 35 Leu Pro Xaa Gly Gln Leu Gln Pro Pro Pro Pro Ile Thr Glu Glu Asp . .55 50 Ala Gln Asp Met Asp Ala Tyr Thr Leu Ala Lys Ala Tyr Phe Asp Val

Lys Glu Tyr Asp Arg Ala Ala His Phe Leu His Gly Cys Asn Ser Lys 80 85 90

Lys Ala Tyr Phe Leu Tyr Met Tyr Ser Arg Tyr Leu Val Arg Ala Ile 95 100 105

Leu Lys Cys His Ser Ala Phe Ser Glu Thr Ser Ile Phe Arg Thr Asn 110 115 120

70

Gly Lys Val Lys Ser Phe Lys 125 130

65

<210> 201 <211> 228 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -25..-1

WO 99/31236 -144- PCT/IB98/02122.

Leu Met Ile Thr Ala Ile Leu Leu Gly Phe Leu Gly Leu Leu Gly 65 Ile Ala Gly Leu Arg Cys Thr Asn Ile Gly Gly Leu Glu Leu Ser Arg 80 Lys Ala Lys Leu Ala Ala Thr Ala Gly Ala Pro His Ile Leu Ala Gly 95 Ile Cys Gly Met Val Ala Ile Ser Trp Tyr Ala Phe Asn Ile Thr Arg 115 110 Asp Phe Phe Asp Pro Leu Tyr Pro Gly Thr Lys Tyr Glu Leu Gly Pro 125 130 Ala Leu Tyr Leu Gly Trp Ser Ala Ser Leu Ile Ser Ile Leu Gly Gly 145 140 Leu Cys Leu Cys Ser Ala Cys Cys Cys Gly Ser Asp Glu Asp Pro Ala 155 160. Ala Ser Ala Arg Arg Pro Tyr Gln Ala Pro Val Ser Val Met Pro Val 170 175 Ala Thr Ser Asp Gln Glu Gly Asp Ser Ser Phe Gly Lys Tyr Gly Arg 195 190 Asn Ala Tyr Val

<210> 202 <211> 64 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -47..-1

<210> 203 <211> 146 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -31..-1

<210> 204 <211> 87 <212> PRT <213> Homo sapiens

. .

<210> 205 <211> 40 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -27..-1

85

<210> 206 <211> 154 <212> PRT <213> Homo sapiens

<400> 206 Met Gly Ser Leu Ser Gly Leu Arg Leu Ala Ala Gly Ser Cys Phe Arg WO 99/31236

10 Leu Cys Glu Arg Asp Val Ser Ser Ser Leu Arg Leu Thr Arg Ser Ser 25 30 Asp Leu Lys Arg Ile Asn Gly Phe Cys Thr Lys Pro Gln Glu Ser Pro Gly Ala Pro Ser Arg Thr Tyr Asn Arg Val Pro Leu His Lys Pro Thr 55 Asp Trp Gln Lys Lys Ile Leu Ile Trp Ser Gly Arg Phe Lys Lys Glu . 75 70 Asp Glu Ile Pro Glu Thr Val Ser Leu Glu Met Leu Asp Ala Ala Lys 85 90 Asn Lys Met Arg Val Lys Ser Ser Tyr Leu Met Ile Ala Leu Thr Val 1,05 Val Gly Cys Ile Phe Met Val Ile Glu Gly Lys Lys Ala Ala Gln Arg 120 His Glu Thr Leu Thr Ser Leu Asn Leu Glu Lys Lys Ala Arg Leu Lys 140 135 Glu Glu Ala Ala Met Lys Ala Lys Thr Glu 150

<210> 207 <211> 101 <212> PRT <213> Homo sapiens

 <400> 207

 Met Val Cys Glu Lys Cys Glu Lys Lys Leu Gly Thr Val Ile Thr Pro

 1
 5
 10
 15

 Asp Thr Trp Lys Asp Gly Ala Arg Asn Thr Thr Glu Ser Gly Gly Arg
 20
 25
 30

 Lys Leu Asn Lys Asn Lys Ala Leu Thr Ser Lys Lys Ala Arg Phe Asp
 35
 40
 45

 Pro Tyr Gly Lys Asn Lys Phe Ser Thr Cys Arg Ile Cys Lys Ser Ser
 50
 55
 60

 Val His Gln Pro Gly Ser His Tyr Cys Gln Gly Cys Ala Tyr Lys Lys
 65
 70
 75
 80

 Gly Ile Cys Ala Met Cys Gly Lys Lys Lys Val Leu Asp Thr Lys Asn Tyr
 85
 90
 95

 Lys Gln Thr Ser Val
 100
 10
 10
 10
 10

<210> 208
<211> 456
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1

```
35
Glu Glu Glu Glu Glu Arg Lys Lys Cys Pro Lys Lys Ala Ser
                                               55
                           50
Phe Ala Ser Ala Ser Ala Glu Val Gly Lys Lys Gly Lys Lys Cys
                        65
Gln Lys Gln Gly Pro Pro Cys Ser Asp Ser Glu Glu Glu Val Glu Arg
                                        85
                    80
Lys Lys Lys Cys His Lys Gln Ala Leu Val Gly Ser Asp Ser Ala Glu
                                    100
Asp Glu Lys Arg Lys Cys Gln Lys His Ala Pro Ile Asn Ser
                                115
            110
Ala Gln His Leu Asp Asn Val Asp Gln Thr Gly Pro Lys Ala Trp Lys
        125
                            130
Gly Ser Thr Thr Asn Asp Pro Pro Lys Gln Ser Pro Gly Ser Thr Ser
                                            150
                        145
Pro Lys Pro Pro His Thr Leu Ser Arg Lys Gln Trp Arg Asn Arg Gln
                                        165
                    160
Lys Asn Lys Arg Arg Cys Lys Asn Lys Phe Gln Pro Pro Gln Val Pro
                                    180
                175
 Asp Gln Ala Pro Ala Glu Ala Pro Thr Glu Lys Thr Glu Val Ser Pro
                                195
            190
 Val Pro Arg Thr Asp Ser His Gly Ala Arg Ala Gly Ala Leu Arg Ala
                            210
                                                215
 Arg Met Ala Gln Arg Leu Asp Gly Ala Arg Phe Arg Tyr Leu Asn Glu
                        225
 Gln Leu Tyr Ser Gly Pro Ser Ser Ala Ala Gln Arg Leu Phe Gln Glu
                    240
                                        245
 Asp Pro Glu Ala Phe Leu Leu Tyr His Arg Gly Phe Gln Ser Gln Val
                                    260
                255
 Lys Lys Trp Pro Leu Gln Pro Val Asp Arg Ile Ala Arg Asp Leu Arg
                                275
             270
 Gln Arg Pro Ala Ser Leu Val Val Ala Asp Phe Gly Cys Gly Asp Cys
                                                295
                            290
 Arg Leu Ala Ser Ser Ile Arg Asn Pro Val His Cys Phe Asp Leu Ala
                                            310
                         305
 Ser Leu Asp Pro Arg Val Thr Val Cys Asp Met Ala Gln Val Pro Leu
                     320
 Glu Asp Glu Ser Val Asp Val Ala Val Phe Cys Leu Ser Leu Met Gly
                                     340
                 335
 Thr Asn Ile Arg Asp Phe Leu Glu Glu Ala Asn Arg Val Leu Lys Pro
             350
 Gly Gly Leu Leu Lys Val Ala Glu Val Ser Ser Arg Phe Glu Asp Val
                             370
 Arg Thr Phe Leu Arg Ala Val Thr Lys Leu Gly Phe Lys Ile Val Ser
                                             390
                         385
 Lys Asp Leu Thr Asn Ser His Phe Phe Leu Phe Asp Phe Gln Lys Thr
                                         405
                     400
 Gly Pro Pro Leu Val Gly Pro Lys Ala Gln Leu Ser Gly Leu Gln Leu
                                     420
                  415
  Gln Pro Cys Leu Tyr Lys Arg Arg
              430
```

<210> 209 <211> 98 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<222> -17..-1

Met Pro Ser Ser Phe Phe Leu Leu Gln Phe Phe Leu Arg Ile Asp -10 Gly Val Leu Ile Arg Met Asn Asp Thr Arg Leu Tyr His Glu Ala Asp 10 5 Lys Thr Tyr Met Leu Arg Glu Tyr Thr Ser Arg Glu Ser Lys Ile Ser 20 25 Ser Leu Met His Val Pro Pro Ser Leu Phe Thr Glu Pro Asn Glu Ile 40 Ser Gln Tyr Leu Pro Ile Lys Glu Ala Val Cys Glu Lys Leu Ile Phe 55 Pro Glu Arg Ile Asp Pro Asn Pro Ala Asp Ser Gln Lys Ser Thr Gln 70 Val Glu 80

<210> 210 <211> 83 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -29..-1

<210> 211 <211> 229 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -23..-1

50 45 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr 65 Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe 80 Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn 100 95 Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr 115 110 Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile 130 125 Ser Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu 145 Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe 165 160 Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val 180 175 Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys 195 190 Arg Lys Ser Arg Thr 205

<210> 212 <211> 152 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -21..-1

Met Ala Gln Leu Gly Ala Val Val Ala Val Ala Ser Ser Phe Phe Cys <400> 212 -10 -15 Ala Ser Leu Phe Ser Ala Val His Lys Ile Glu Glu Gly His Ile Gly Val Tyr Tyr Arg Gly Gly Ala Leu Leu Thr Ser Thr Ser Gly Pro Gly 20 Phe His Leu Met Leu Pro Phe Ile Thr Ser Tyr Lys Ser Val Gln Thr 35 Thr Leu Gln Thr Asp Glu Val Lys Asn Val Pro Cys Gly Thr Ser Gly 50 Gly Val Met Ile Tyr Phe Asp Arg Ile Glu Val Val Asn Phe Leu Val 70 65 Pro Asn Ala Val His Asp Ile Val Lys Asn Tyr Thr Ala Asp Tyr Asp 85 Lys Ala Leu Ile Phe Asn Lys Ile His His Glu Leu Asn Gln Phe Cys 100 Ser Val His Thr Leu Gln Glu Val Tyr Ile Glu Leu Phe Gly Leu Glu 115 110 Asn Asp Phe Ser Gln Glu Ser Ser

130

<210> 213 <211> 179 <212> PRT <213> Homo sapiens

<220>

```
<221> SIGNAL
<222> -54..-1
<400> 213
Met Ala Ala Ser Glu Ala Ala Val Val Ser Ser Pro Ser Leu Lys Thr
               -50
                                    -45
Asp Thr Ser Pro Val Leu Glu Thr Ala Gly Thr Val Ala Ala Met Ala
                                -30
Ala Thr Pro Ser Ala Arg Ala Ala Ala Ala Val Ala Ala Ala Ala
                            -15
Arg Thr Gly Ser Glu Ala Arg Val Ser Lys Ala Ala Leu Ala Thr Lys
Leu Leu Ser Leu Ser Gly Val Phe Ala Val His Lys Pro Lys Gly Pro
Thr Ser Ala Glu Leu Leu Asn Arg Leu Lys Glu Lys Leu Leu Ala Glu
                                35
Ala Gly Met Pro Ser Pro Glu Trp Thr Lys Arg Lys Lys Gln Thr Leu
                            50
Lys Ile Gly His Gly Gly Thr Leu Asp Ser Ala Ala Arg Gly Val Leu
                        65
Val Val Gly Ile Gly Ser Gly Thr Lys Met Leu Thr Ser Met Leu Ser
                    80
Gly Ser Lys Arg Tyr Thr Ala Ile Gly Glu Leu Gly Lys Ala Thr Asp
                                    100
Thr Leu Asp Ser Thr Gly Lys Val Thr Glu Glu Lys Pro Tyr Gly Met
            110
                                115
Asn Leu Ile
```

<210> 214 <211> 269 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

125

<400> 214

<222> -92..-1

Met Ile Thr His Val Thr Leu Glu Asp Ala Leu Ser Asn Val Asp Leu -85 Leu Glu Glu Leu Pro Leu Pro Asp Gln Gln Pro Cys Ile Glu Pro Pro -70 Pro Ser Ser Ile Met Tyr Gln Ala Asn Phe Asp Thr Asn Phe Glu Asp -55 -50 Arg Asn Ala Phe Val Thr Gly Ile Ala Arg Tyr Ile Glu Gln Ala Thr Val His Ser Ser Met Asn Glu Met Leu Glu Glu Gly His Glu Tyr Ala -25 -20 Val Met Leu Tyr Thr Trp Arg Ser Cys Ser Arg Ala Ile Pro Gln Val -5 Lys Cys Asn Glu Gln Pro Asn Arg Val Glu Ile Tyr Glu Lys Thr Val Glu Val Leu Glu Pro Glu Val Thr Lys Leu Met Lys Phe Met Tyr Phe Gln Arg Lys Ala Ile Glu Arg Phe Cys Ser Glu Val Lys Arg Leu Cys His Ala Glu Arg Arg Lys Asp Phe Val Ser Glu Ala Tyr Leu Leu Thr

Leu Gly Lys Phe Ile Asn Met Phe Ala Val Leu Asp Glu Leu Lys Asn Met Lys Cys Ser Val Lys Asn Asp His Ser Ala Tyr Lys Arg Ala Ala 90 95 Gln Phe Leu Arg Lys Met Ala Asp Pro Gln Ser Ile Gln Glu Ser Gln 105 110 Asn Leu Ser Met Phe Leu Ala Asn His Asn Arg Ile Thr Gln Cys Leu 120 125 His Gln Gln Leu Glu Val Ile Pro Gly Tyr Glu Glu Leu Leu Ala Asp 145 140 Ile Val Asn Ile Cys Val Asp Tyr Tyr Glu Asn Lys Met Tyr Leu Thr 160 155 Pro Ser Glu Lys His Met Leu Leu Lys Val Lys Leu Pro 170 165

<210> 215 <211> 135 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -22..-1

<400> 215

Met Gln Thr Val Tyr Tyr Gly Ser Leu Gly Leu Trp Leu Ala Leu Val -15 -10 Asp Gly Leu Val Arg Ser Ser Pro Ser Leu Asp Gln Met Phe Asp Ala Glu Ile Leu Gly Phe Ser Thr Pro Pro Gly Arg Leu Ser Met Met Ser 15 20 Phe Ile Phe Asn Ala Leu Thr Cys Ala Leu Gly Leu Leu Tyr Phe Ile 35 Arg Arg Gly Lys Gln Cys Leu Asp Phe Thr Val Thr Val His Phe Phe His Leu Leu Gly Cys Trp Phe Tyr Ser Ser Arg Phe Pro Ser Ala Leu Thr Trp Trp Leu Val Gln Ala Val Cys Ile Ala Leu Met Ala Val Ile 80 85 Gly Glu Tyr Leu Cys Met Arg Thr Glu Leu Lys Glu Ile Pro Leu Asn 95

Ser Ala Pro Lys Ser Asn Val 110

<210> 216 <211> 67 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -38..-1

<400> 216

Met Asn Asn Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser
-35 -30 -25

Val Lys Gly His Val Lys Met Leu Arg Leu Val Phe Ala Leu Val Thr
-20 -15 -10

Ala Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu -5 1 5 10

Phe Asn Pro Asn Gly Pro Tyr Gln Lys Lys Pro Val His Glu Lys Lys 15 20 25

Glu Val Leu

<210> 217 <211> 125 <212> PRT <213> Homo sapiens

<221> SIGNAL <222> -54..-1

<400> 217

 Met Ala Asp Glu Glu Leu Glu Ala Leu Arg Arg Gln Arg Leu Ala Glu -50

 Leu Gln Ala Lys His Gly Asp Pro Gly Asp Ala Ala Gln Gln Glu Ala -35

 Lys His Arg Glu Ala Glu Met Arg Asn Ser Ile Leu Ala Gln Val Leu -20

 Asp Gln Ser Ala Arg Ala Arg Leu Ser Asn Leu Ala Leu Val Lys Pro -5

 Glu Lys Thr Lys Ala Val Glu Asn Tyr Leu Ile Gln Met Ala Arg Tyr 15

 Gly Gln Leu Ser Glu Lys Val Ser Glu Gln Gly Leu Ile Glu Ile Leu 30

 Lys Lys Val Ser Gln Gln Thr Glu Lys Thr Thr Thr Val Lys Phe Asn 45

 Arg Arg Lys Val Met Asp Ser Asp Glu Asp Asp Asp Tyr 70

<210> 218
<211> 376
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 218

 Met
 Gly
 His
 Arg
 Phe
 Leu
 Arg
 Gly
 Leu
 Leu
 Thr
 Leu
 Leu
 Pro
 Pro
 Pro
 Pro
 Pro
 Leu
 Tyr
 Thr
 Arg
 His
 Arg
 Met
 Leu
 Gly
 Pro
 Glu
 Ser
 Val
 Pro

 Pro
 Pro
 Lys
 Arg
 Ser
 Lys
 Leu
 Met
 Ala
 Pro
 Pro
 Arg
 Ile
 Gly

 Pro
 Pro
 Lys
 Arg
 Ser
 Lys
 Leu
 Met
 Ala
 Pro
 Pro
 Arg
 Ile
 Gly

 Pro
 Pro
 Interverse
 Interverse

```
100
 Leu Ser Ser Ala Gly Leu Ile Tyr Leu His Phe Gly His Lys Leu Leu
        110
                    115
                                   .
                                              120
 Ala Gln Leu Leu Gly Thr Ser Glu Glu Asp Ser Met Val Gly Thr Leu
                       130
 Tyr Asp Lys Met Tyr Glu Asn Phe Val Glu Val Asp Ala Val Asp
                    145
                                       150
 Asn Gly Ile Ser Gln Trp Ala Glu Gly Glu Pro Arg Tyr Ala Leu Thr
                160
                                   165
 Thr Thr Leu Ser Ala Arg Val Ala Arg Leu Asn Pro Thr Trp Asn His
            175
                                180
 Pro Asp Gln Asp Thr Glu Ala Gly Phe Lys Arg Ala Met Asp Leu Val
        190
                            195
                                               200
''Gln Glu Glu Phe Leu Gln Arg Leu Asp Phe Tyr Gln His Ser Trp Leu
                       210
                                          215
 Pro Ala Arg Ala Leu Val Glu Glu Ala Leu Ala Gln Arg Phe Gln Val
                    225
                                       230
 Asp Pro Ser Gly Glu Ile Val Glu Leu Ala Lys Gly Ala Cys Pro Trp
                240
                                   245
 Lys Glu His Leu Tyr His Leu Glu Ser Gly Leu Ser Pro Pro Val Ala
            255
                               260
 Ile Phe Phe Val Ile Tyr Thr Asp Gln Ala Gly Gln Trp Arg Ile Gln
                            275
                                              280
 Cys Val Pro Lys Glu Pro His Ser Phe Gln Ser Arg Leu Pro Leu Pro
                       290
                                          295
 Glu Pro Trp Arg Gly Leu Arg Asp Glu Ala Leu Asp Gln Val Ser Gly
                    305
                                      310
 Ile Pro Gly Cys Ile Phe Val His Ala Ser Gly Phe Ile Gly Gly His
                                         * *
                320
                                   325
 Arg Thr Arg Glu Gly Ala Leu Ser Met Ala Arg Ala Thr Leu Ala Gln
                                340
 Arg Ser Tyr Leu Pro Gln Ile Ser
         350
```

<210> 219 <211> 211 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -30..-1

<400> 219

Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His Leu Leu Val -25 -20 Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala Ala Pro -10 -5 Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu Thr Gly Leu 10 Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys Gly Asn Leu 25 3.0 Leu Arg Gly Ile Asp Ser Leu Phe Ser Ala Pro Met Asp Phe Arg Gly Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His Gln Leu Gly 60 Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Val Pro Arg Met 75 Glu Glu Lys Glu Ala Leu Val Pro Ile Gln Lys Ala Thr Asp Ser Phe 90

His Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile Lys Leu Pro 105 . 110 Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His Trp Leu Ser 115 120 125 Glu Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu Arg Lys Gly 135 140 Thr His Lys Asp Val Leu Glu Glu Gly Thr Glu Ser Ser His Ser 155 Arg Leu Ser Pro Arg Lys Thr His Leu Leu Tyr Ile Leu Arg Pro Ser 170 175 Arg Gln Leu 180

<211> 154 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -60..-1 <400> 220 Met Gly Ser Lys Cys Cys Lys Gly Gly Pro Asp Glu Asp Ala Val Glu -55 -50 Arg Gln Arg Arg Gln Lys Leu Leu Leu Ala Gln Leu His His Arg Lys -35 -30 -40 Arg Val Lys Ala Ala Gly Gln Ile Gln Ala Trp Trp Arg Gly Val Leu -20 Val Arg Arg Thr Leu Leu Val Ala Ala Leu Arg Ala Trp Met Ile Gln - 5 Cys Trp Trp Arg Thr Leu Val Gln Arg Arg Ile Arg Gln Arg Arg Gln 10 Ala Leu Leu Arg Val Tyr Val Ile Gln Glu Gln Ala Thr Val Lys Leu 30 Gln Ser Cys Ile Arg Met Trp Gln Cys Arg Gln Cys Tyr Arg Gln Met 45

Cys Asn Ala Leu Cys Leu Phe Gln Val Pro Glu Ser Ser Leu Ala Phe
55 60 65
Gln Thr Asp Gly Phe Leu Gln Val Gln Tyr Ala Ile Pro Ser Lys Gln

75

Pro Glu Phe His Ile Glu Ile Leu Ser Ile

<210> 221 <211> 123 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -42..-1

<210> 220

Ala Val Ser Leu Ser Ala Pro Ala Phe Ala Ser Ala Leu Arg Ser Met
-10
Lys Ser Ser Gln Ala Ala Arg Lys Asp Asp Phe Leu Arg Ser Leu Ser
10
Asp Gly Asp Ser Gly Thr Ser Glu His Ile Ser Ala Val Val Thr Ser
25
Pro Arg Ile Ser Cys His Gly Ala Ala Ile Pro Thr Ala Arg Ala Leu
40
Cys Leu Gly Cys Ser Cys Cys Thr Glu Arg Leu Leu Pro Pro
55
Ser Leu Leu Ser Leu Glu Ala Pro Ala Ser Thr
75

<210> 222 <211> 346 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 <400> 222 Met Ala Met Ala Gln Lys Leu Ser His Leu Leu Pro Ser Leu Arg Gln -10 -15 Val Ile Gln Glu Pro Gln Leu Ser Leu Gln Pro Glu Pro Val Phe Thr 1 . . Val Asp Arg Ala Glu Val Pro Pro Leu Phe Trp Lys Pro Tyr Ile Tyr 25 20 Ala Gly Tyr Arg Pro Leu His Gln Thr Trp Arg Phe Tyr Phe Arg Thr . 35 Leu Phe Gln Gln His Asn Glu Ala Val Asn Val Trp Thr His Leu Leu 55 Ala Ala Leu Val Leu Leu Leu Arg Leu Ala Leu Phe Val Glu Thr Val 70 Asp Phe Trp Gly Asp Pro His Ala Leu Pro Leu Phe Ile Ile Val Leu 85 Ala Ser Phe Thr Tyr Leu Ser Leu Ser Ala Leu Ala His Leu Leu Gln 100 Ala Lys Ser Glu Phe Trp His Tyr Ser Phe Phe Phe Leu Asp Tyr Val 120 115 Gly Val Ala Val Tyr Gln Phe Gly Ser Ala Leu Ala His Phe Tyr Tyr 135 130 Ala Ile Glu Pro Ala Trp His Ala Gln Val Gln Ala Val Phe Leu Pro 150 Met Ala Ala Phe Leu Ala Trp Leu Ser Cys Ile Gly Ser Cys Tyr Asn 170 165 Lys Tyr Ile Gln Lys Pro Gly Leu Leu Gly Arg Thr Cys Gln Glu Val 180 185 Pro Ser Val Leu Ala Tyr Ala Leu Asp Ile Ser Pro Val Val His Arg 200 195 Ile Phe Val Ser Ser Asp Pro Thr Thr Asp Asp Pro Ala Leu Leu Tyr 215 210 His Lys Cys Gln Val Val Phe Phe Leu Leu Ala Ala Ala Phe Phe Ser 230 Thr Phe Met Pro Glu Arg Trp Phe Pro Gly Ser Cys His Val Phe Gly 245 Gln Gly His Gln Leu Phe His Ile Phe Leu Val Leu Cys Thr Leu Ala 260 Gln Leu Glu Ala Val Ala Leu Asp Tyr Glu Ala Arg Arg Pro Ile Tyr

<210> 223
<211> 210
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1

<400> 223 Met Asp Asn Arg Phe Ala Thr Ala Phe Val Ile Ala Cys Val Leu Ser -15 -10 Leu Ile Ser Thr Ile Tyr Met Ala Ala Ser Ile Gly Thr Asp Phe Trp Tyr Glu Tyr Arg Ser Pro Val Gln Glu Asn Ser Ser Asp Leu Asn Lys 20 Ser Ile Trp Asp Glu Phe Ile Ser Asp Glu Ala Asp Glu Lys Thr Tyr 35 40 Asn Asp Ala Leu Phe Arg Tyr Asn Gly Thr Val Gly Leu Trp Arg Arg 50 55 Cys Ile Thr Ile Pro Lys Asn Met His Trp Tyr Ser Pro Pro Glu Arg 70 Thr Glu Ser Phe Asp Val Val Thr Lys Cys Val Ser Phe Thr Leu Thr 85

Glu Gln Phe Met Glu Lys Phe Val Asp Pro Gly Asn His Asn Ser Gly
95 100 105

Ile Asp Leu Leu Arg Thr Tyr Leu Trp Arg Cys Gln Phe Leu Leu Pro

Ile Asp Leu Leu Arg Thr Tyr Leu Trp Arg Cys Gln Phe Leu Leu Pro
110 115 120

Phe Val Ser Leu Gly Leu Met Cys Phe Gly Ala Leu Ile Gly Leu Cys 125 130 135 140 Ala Cys Ile Cys Arg Ser Leu Tyr Pro Thr Ile Ala Thr Gly Ile Leu

145 150 155
His Leu Leu Ala Val Thr Lys Glu Ser Met Leu Pro Ala Gly Ala Glu

160 165 170 Ser Lys His Thr Ala Thr Pro Ala His Ala Cys Val Gln Thr Gly Lys

180

Pro Lys 190

<210> 224 <211> 184 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -20..-1

<400> 224

Met Asp Asn Arg Phe Ala Thr Ala Phe Val Ile Ala Cys Val Leu Ser

WO 99/31236

-10 -15 -20 Leu Ile Ser Thr Ile Tyr Met Ala Ala Ser Ile Gly Thr Asp Phe Trp Tyr Glu Tyr Arg Ser Pro Val Gln Glu Asn Ser Ser Asp Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser Asp Glu Ala Asp Glu Lys Thr Tyr 35 Asn Asp Ala Pro Phe Arg Tyr Asn Gly Thr Val Gly Leu Trp Arg Arg 55 Cys Ile Thr Ile Pro Lys Asn Met His Trp Tyr Ser Pro Pro Glu Arg 70 Thr Glu Ser Phe Asp Val Val Thr Lys Cys Val Ser Phe Thr Leu Thr 85 Glu Gln Phe Met Glu Lys Phe Val Asp Pro Gly Asn His Asn Ser Gly 100 Ile Asp Leu Leu Arg Thr Tyr Leu Trp Arg Cys Gln Phe Leu Leu Pro 115 Phe Val Ser Leu Gly Leu Met Cys Phe Gly Ala Leu Ile Gly Leu Cys 135 130 Ala Cys Ile Cys Arg Ser Leu Tyr Pro Thr Ile Ala Thr Gly Ile Leu 145 150 His Leu Leu Ala Asp Thr Met Leu

<210> 225
<211> 227
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1

<400> 225 Met Gly Trp Thr Met Arg Leu Val Thr Ala Ala Leu Leu Leu Gly Leu -15 Met Met Val Val Thr Gly Asp Glu Asp Glu Asn Ser Pro Cys Ala His Glu Ala Leu Leu Asp Glu Asp Thr Leu Phe Cys Gln Gly Leu Glu Val 20 Phe Tyr Pro Glu Leu Gly Asn Ile Gly Cys Lys Val Val Pro Asp Cys Asn Asn Tyr Arg Gln Lys Ile Thr Ser Trp Met Glu Pro Ile Val Lys 50 Phe Pro Gly Ala Val Asp Gly Ala Thr Tyr Ile Leu Val Met Val Asp 65 Pro Asp Ala Pro Ser Arg Ala Glu Pro Arg Gln Arg Phe Trp Arg His 80 85 Trp Leu Val Thr Asp Ile Lys Gly Ala Asp Leu Lys Lys Gly Lys Ile 100 Gln Gly Gln Glu Leu Ser Ala Tyr Gln Ala Pro Ser Pro Pro Ala His 115 Ser Gly Phe His Arg Tyr Gln Phe Phe Val Tyr Leu Gln Glu Gly Lys Val Ile Ser Leu Leu Pro Lys Glu Asn Lys Thr Arg Gly Ser Trp Lys 145 Met Asp Arg Phe Leu Asn Arg Phe His Leu Gly Glu Pro Glu Ala Ser 165 160 Thr Gln Phe Met Thr Gln Asn Tyr Gln Asp Ser Pro Thr Leu Gln Ala 180

```
Pro Arg Glu Arg Ala Ser Glu Pro Lys His Lys Asn Gln Ala Glu Ile
190 195 200
Ala Ala Cys
205
```

```
<210> 226
<211> 74
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -41..-1
<400> 226
Met Ile Ala Arg Arg Asn Pro Val Pro Leu Arg Phe Leu Pro Asp Glu
                       -35
                                            -30
Ala Arg Ser Leu Pro Pro Pro Lys Leu Thr Asp Pro Arg Leu Leu Tyr
                -20
                                                           -10
                                       -15
Ile Gly Phe Leu Gly Tyr Cys Ser Gly Leu Ile Asp Asn Leu Ile Arg
               -5
                                   1
```

Arg Arg Pro Ile Ala Thr Ala Gly Leu His Arg Gln Leu Leu Tyr Ile
10 15 20

Thr Ala Phe Phe Leu Leu Asp Ile Ile Leu
25 30

<210> 227 <211> 73 <212> PRT <213> Homo sapiens

Lys Lys Phe Leu Glu Ser Asp Asp Lys Met Val Lys Lys Ile Ala
35 40 45

Met Arg Glu Val Lys Leu Leu Lys Gln Leu Arg His Glu Asn Leu Val 50 55 60

Asn Leu Leu Glu Val Cys Lys Lys 65 70

<210> 228 <211> 82 <212> PRT <213> Homo sapiens <220>

<400> 228

<221> SIGNAL <222> -16..-1

Met Lys Arg Leu Leu Pro Ala Thr Ser Leu Ala Gly Pro Val Leu Ser
-15
-10
-5
Thr Leu Ile Ala Pro Thr Pro Met Leu Phe Cys Glu Asp Lys Ser Trp

<210> 229
<211> 119
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -56..-1

<400> 229 Met Ala Glu Pro Ser Ala Ala Thr Gln Ser His Ser Ile Ser Ser Ser -45 -50 Ser Phe Gly Ala Glu Pro Ser Ala Pro Gly Gly Gly Ser Pro Gly -35 -30 Ala Cys Pro Ala Leu Gly Thr Lys Ser Cys Ser Ser Ser Cys Ala Asp -20 -15 Ser Phe Val Ser Ser Ser Ser Gln Pro Val Ser Leu Phe Ser Thr 1 -5 Ser Gln Glu Gly Leu Ser Ser Leu Cys Ser Asp Glu Pro Ser Ser Glu 20 15 Ile Met Thr Ser Ser Phe Leu Ser Ser Ser Glu Ile His Asn Thr Gly 30 35 Leu Thr Ile Leu His Gly Glu Lys Ser His Val Leu Gly Ser Gln Pro 50 45 Ile Leu Ala Lys Lys Lys

<210> 230 <211> 54 <212> PRT <213> Homo sapiens

60

 Ala Phe Val
 Trp Glu
 Pro Ala Met Val
 Arg Ile Asn Ala Leu
 Thr Ala

 1
 5
 5
 10
 15

 Ala Ser Glu
 Ala Ala Cys Leu
 Ile Val
 Ser Val
 Asp Glu
 Thr Ile Lys

 20
 25
 30

 Asn Pro Arg
 Ser Thr Val
 Asp Ala Pro Thr Ala Ala Gly
 Arg Gly
 Arg Gly
 Arg

 Gly Arg Gly
 Arg Pro His
 50

<210> 231 <211> 210 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> ~14..-1

<400> 231 Met Leu Thr Leu Leu Gly Leu Ser Phe Ile Leu Ala Gly Leu Ile Val -10 - 5 Gly Gly Ala Cys Ile Tyr Lys Tyr Phe Met Pro Lys Ser Thr Ile Tyr 10 Arg Gly Glu Met Cys Phe Phe Asp Ser Glu Asp Pro Ala Asn Ser Leu 25 Arg Gly Gly Glu Pro Asn Phe Leu Pro Val Thr Glu Glu Ala Asp Ile 40 45 Arg Glu Asp Asp Asn Ile Ala Ile Ile Asp Val Pro Val Pro Ser Phe 60 Ser Asp Ser Asp Pro Ala Ala Ile Ile His Asp Phe Glu Lys Gly Met 75 Thr Ala Tyr Leu Asp Leu Leu Leu Gly Ile Cys Tyr Leu Met Pro Leu 90 Asn Thr Ser Ile Val Met Pro Pro Lys Asn Leu Val Glu Leu Phe Gly 110 105 Lys Leu Ala Ser Gly Arg Tyr Leu Pro Gln Thr Tyr Val Val Arg Glu 120 125 Asp Leu Val Ala Val Glu Glu Ile Arg Asp Val Ser Asn Leu Gly Ile 135 140 , Phe Ile Tyr Gln Leu Cys Asn Asn Arg Lys Ser Phe Arg Leu Arg Arg 150 155 Arg Asp Leu Leu Cly Phe Asn Lys Arg Ala Ile Asp Lys Cys Trp 170 175 Lys Ile Arg His Phe Pro Asn Glu Phe Ile Val Glu Thr Lys Ile Cys 185 Gln Glu 195

<210> 232 <211> 108 <212> PRT <213> Homo sapiens

<400> 232

 Met
 Gly
 Cys
 Val
 Phe
 Gln
 Ser
 Thr
 Glu
 Asp
 Lys
 Cys
 Ile
 Phe
 Lys
 Ile

 1
 5
 10
 10
 15
 15

 Asp
 Trp
 Thr
 Leu
 Ser
 Pro
 Glu
 His
 Ala
 Lys
 Asp
 Glu
 Tyr
 Val
 Leu
 Ser
 Val
 Pro
 Ile
 Gly
 Asp
 Glu
 Asp
 Asp
 Asp
 Fro
 Gly
 Asp
 Gly
 Asp
 Asp
 Asp
 Ile
 Leu
 Cys
 Asp
 Gly
 Asp
 Asp
 Asp
 Asp
 Asp
 Ile
 Asp
 Asp
 Ile
 Asp
 Asp
 Ile
 Asp
 <t

```
<212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -18..-1
 <400> 233
 Met Ser Ser Gly Arg Leu Arg Trp Leu Met Pro Val Ile Pro Ala Leu
           -15
                                -10
 Trp Gly Ala Glu Lys Gly Glu Ser Pro Glu Val Ser Ser Phe Glu Thr
                    5
 Arg Leu Ala Asn Met Ala Lys Pro Cys Leu Tyr
15
                    20
 <210> 234
 <211> 36
 <212> PRT
 <213> Homo sapiens
 Met Ser Ala Arg Ile Pro Phe Tyr Lys Asp Thr Ser Gln Ile Arg Leu
                                    10
 Gly Ser Thr Ile Ile Pro His Phe Asn Leu Ile Thr Phe Val Lys Thr
            20
                                25
Phe Phe Gln Ile
       35
 <210> 235
 <211> 307
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -13..-1
 <400> 235
 Met Leu Ala Val Ser Leu Thr Val Pro Leu Leu Gly Ala Met Met Leu
                                -5
 Leu Glu Ser Pro Ile Asp Pro Gln Pro Leu Ser Phe Lys Glu Pro Pro
                        10
 Leu Leu Gly Val Leu His Pro Asn Thr Lys Leu Arg Gln Ala Glu
                    25
                                        30
 Arg Leu Phe Glu Asn Gln Leu Val Gly Pro Glu Ser Ile Ala His Ile
                40
                                    45
 Gly Asp Val Met Phe Thr Gly Thr Ala Asp Gly Arg Val Val Lys Leu
 Glu Asn Gly Glu Ile Glu Thr Ile Ala Arg Phe Gly Ser Gly Pro Cys
                            75
 Lys Thr Arg Asp Asp Glu Pro Val Cys Gly Arg Pro Leu Gly Ile Arg
                        90
```

Ala Gly Pro Asn Gly Thr Leu Phe Val Ala Asp Ala Cys Lys Gly Leu

Phe Glu Val Asn Pro Trp Lys Arg Glu Val Lys Leu Leu Ser Ser

Glu Thr Pro Ile Glu Gly Lys Asn Met Ser Phe Val Asn Asp Leu Thr
135 140 145

110

125

105

Val Ser Gln Asp Gly Arg Lys Ile Tyr Phe Thr Asp Ser Ser Ser Lys 155 160 Trp Gln Arg Arg Asp Tyr Leu Leu Leu Val Met Glu Gly Thr Asp Asp 170 175 Gly Arg Leu Leu Glu Tyr Asp Thr Val Thr Arg Glu Val Lys Val Leu 185 190 Leu Asp Gln Leu Arg Phe Pro Asn Gly Val Gln Leu Ser Pro Ala Glu 200 205 Asp Phe Val Leu Val Ala Glu Thr Thr Met Ala Arg Ile Arg Arg Val 220 Tyr Val Ser Gly Leu Met Lys Gly Gly Ala Asp Leu Phe Val Glu Asn 230 235 . . Met Pro Gly Phe Pro Asp Asn Ile Arg Pro Ser Ser Ser Gly Gly Tyr 250 255 Trp Val Gly Met Ser Thr Ile Arg Pro Asn Pro Gly Phe Ser Met Leu 265 270 275 Asp Phe Leu Ser Glu Arg Pro Trp Ile Lys Arg Met Ile Phe Lys Ala 285 Lys Lys Lys

<210> 236 <211> 106 <212> PRT <213> Homo sapiens <220> <221> SIGNAL "" <222> -32..-1

<400> 236

Met Phe Ala Pro Ala Val Met Arg Ala Phe Arg Lys Asn Lys Thr Leu -30 -25 -20 Gly Tyr Gly Val Pro Met Leu Leu Leu Ile Val Gly Gly Ser Phe Gly -10 -5 Leu Arg Glu Phe Ser Gln Ile Arg Tyr Asp Ala Val Lys Ser Lys Met 10 Asp Pro Glu Leu Glu Lys Lys Leu Lys Glu Asn Lys Ile Ser Leu Glu 25 Ser Glu Tyr Glu Lys Ile Lys Asp Ser Lys Phe Asp Asp Trp Lys Asn 40 Ile Arg Gly Pro Arg Pro Trp Glu Asp Pro Asp Leu Leu Gln Gly Arg 55 Asn Pro Glu Ser Leu Lys Thr Lys Thr Thr

<210> 237 <211> 42 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1

Met Asp Leu Arg Gln Phe Leu Met Cys Leu Ser Leu Cys Thr Ala Phe
-15 -10 -5
Ala Leu Ser Lys Pro Thr Glu Lys Lys Asp Arg Val His His Glu Pro

1 5 10
Gln Leu Ser Asp Lys Val His Asn Asp Ile
20

<210> 238
<211> 117
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20. -1

·<400> 238 Met Asp Asn Arg Phe Ala Thr Ala Phe Val Ile Ala Cys Val Leu Ser -15 Leu Ile Ser Thr Ile Tyr Met Ala Ala Ser Ile Gly Thr Asp Phe Trp Tyr Glu Tyr Arg Ser Pro Val Gln Glu Asn Ser Ser Asp Leu Asn Lys 20 Ser Ile Trp Asp Glu Phe Ile Ser Asp Glu Ala Asp Glu Lys Thr Tyr 35 40 Asn Asp Ala Leu Phe Arg Tyr Asn Gly Thr Val Gly Leu Trp Gly Arg 50 \_ . . 55 Cys Ile Thr Ile Pro Lys Asn Met His Trp Tyr Ser Pro Pro Glu Arg 70 Thr Gly Ile Ser Leu Ile Leu Thr Ser Val Phe Phe Thr Trp Leu Ile Ile Asp Lys Thr Thr 95

<210> 239 <211> 178 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -37..-1

<400> 239 Met Glu Arg Gln Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe -30 Gln His Xaa Xaa Ala Xaa Xaa Leu Leu Val Phe Asn Phe Leu Leu Ile -15 -10 Leu Thr Ile Leu Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe 1 Leu His Glu Thr Gly Gly Ala Met Val Tyr Gly Leu Ile Met Gly Leu 20 Ile Ser Arg Tyr Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Thr Val Cys Asp Cys Val Lys Leu Thr Phe Ser Pro Pro Thr Leu Leu Val Asn 50 Val Thr Asp Gln Val Tyr Glu Tyr Lys Tyr Lys Arg Glu Ile Ser Gln 70 His Asn Ile Asn Pro His Gln Gly Asn Ala Ile Leu Glu Lys Met Thr Phe Asp Pro Glu Ile Phe Phe Asn Val Leu Pro Pro Ile Ile Phe

PCT/IB98/02122 -

```
His Ala Gly Tyr Ser Leu Lys Lys Arg His Phe Phe Gln Asn Leu Gly
110 115 120

Ser Ile Leu Thr Tyr Ala Phe Leu Gly Thr Ala Ile Ser Cys Ile Val
125 130 135

Ile Gly
140
```

```
<210> 240
<211> 126
<212> PRT
<213> Homo sapiens
<220>
```

<221> SIGNAL <222> -27..-1

<400> 240 Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly Val Val -20 -15 Val Leu Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr Glu Ser -5 1 Met Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Ile Phe Ile 10 Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr Met Ala 30 Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys Asp Tyr 45 Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met Lys Gly - 60 Leu Lys Cys Arg Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro 75 Tyr Phe Lys Met His Lys Pro Val Thr Met Lys Lys Lys

<210> 241 <211> 174 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -115..-1 <400> 241 Met Arg Trp Ser Cys

Met Arg Trp Ser Cys Glu His Leu Val Met Val Trp Ile Asn Ala Phe -110 -105 Val Met Leu Thr Thr Gln Leu Leu Pro Ser Lys Tyr Cys Asp Leu Leu -95 -90 His Lys Ser Ala Ala His Leu Gly Lys Trp Gln Lys Leu Glu His Gly -80 -75 Ser Tyr Ser Asn Ala Pro Gln His Ile Trp Ser Glu Asn Thr Ile Trp -60 -55 Pro Gln Gly Val Leu Val Arg His Ser Arg Cys Leu Tyr Arg Ala Met -45 -40 Gly Pro Tyr Asn Val Ala Val Pro Ser Asp Val Ser His Ala Arg Phe -30 -25 Tyr Phe Leu Phe His Arg Pro Leu Arg Leu Leu Asn Leu Leu Ile Leu

-5

-10

11

-15

Ile Glu Gly Gly Val Val Phe Tyr Gln Leu Tyr Ser Leu Leu Arg Ser 5 Glu Lys Trp Asn His Thr Leu Ser Met Ala Leu Ile Leu Phe Cys Asn 20 Tyr Tyr Val Leu. Phe Lys Leu Leu Arg Asp Arg Ile Val Leu Gly Arg 30 35 40 Ala Tyr Ser Tyr Pro Leu Asn Ser Tyr Glu Leu Lys Ala Asn 50 55 .... <210> 242 ... ····<211> 896 .. <212> DNA <213> Homo sapiens <220> <221> CDS <222> 18..173 <221> sig\_peptide <222> 18..77 <223> Von Heijne matrix score 6.5 seq GLCVLQLTTAVTS/AF <221> polyA signal <222> 864..869 <221> polyA\_site <222> 882..893 <400> 242 50 aaccttcaca gtgtgag atg cct agt gtg aac agt gct gga tta tgt gtc Met Pro Ser Val Asn Ser Ala Gly Leu Cys Val -20 -15 98 ttg cag ttg aca acg gca gtr acc agt gcc ttt tta cta gca aaa gtg Leu Gln Leu Thr Thr Ala Val Thr Ser Ala Phe Leu Leu Ala Lys Val -5 1 aat cct ttc gaa rct ttt ctc tca agg ggc ttt tgg cta tgt gcc 146 Asn Pro Phe Glu Xaa Phe Leu Ser Arg Gly Phe Trp Leu Cys Ala Ala 15 cat cat ttc att cat cct tgc ctg gat tgagacgtgt tcctgattca 193 His His Phe Ile His Pro Cys Leu Asp aagtgttacc tcaagaagca gaagaagaaa acagactcct gatagttcag gatgcttcag 253 agagggcagc acttatacct ggtggtcttt ctgatggtca gttttattcc cctcctgaat 313 373 ccgaagcagg atctgaagaa gctgaagaaa aacaggacag tgagaaacca cttttagaac tatgagtact acttttgtta aatgtgaaaa accctcacag aaagtcatcg aggcaaaaaag 433 493 aggcaggcag tggagtctcc ctgtcgacag taaagttgaa atggtgacgt ccactgctgg 553 ctttattgaa cagctaataa agatttattt attgtaatac ctcacagacg ttgtaccata tccatgcaca tttagttgcc tgcctgtggc tggtaaggta atgtcatgat tcatcctctc 613 ttcagtgaga ctgagcctga tgtgttaaca aataggtgaa gaaagtcttg tgctgtattc 673 ctaatcaaaa gacttaatat attgaagtaa cactttttta gtaagcaaga taccttttta 733 tttcaattca cagaatggaa tttttttgtt tcatgtctca gatttatttt gtatttcttt 793 tttaacactc tacatttccc ttgtttttta actcatgcac atgtgctctt tgtacagttt 853 taaaaagtgt aataaaatct gacatgtcaa araaaaaaaa mcy 896

<211 <212 <213	> DI		sapie	ens												
<220 <221 <222	> C1	os 759	95								•					
<222	> 1° > Vo	ig_pe 78: on He core eq FI	5 21jne 3.70	mat	0476		2									•
		olyA_ 208		al				•					•			
	> 84	olyA_ 408							٠.,							
aagg	1999	egt g	9999	c at Me	g gt t Va	g gt	c tt al Le	eu Ai	g gc	g gg	g aa y Ly	ig aa 's Ly -1	s Th	c tt ir Ph	t ctc ne Leu	52
ccc Pro	cct Pro -10	ctm Leu	wgc Xaa	cgc Arg	gcc Ala	ttc Phe -5	gcc Ala	tgc Cys	cgc Arg	ggc	tgt Cys 1	caa Gln	ctc Leu	gct Ala	ccg Pro 5	100
gag Glu	cgc Arg	ggc Gly	gcc Ala	gag Glu 10	cgc Arg	agg Arg	gat Asp	aca Thr	gcg Ala 15	ccc Pro	agc Ser	999 Gly	gtc Val	tca Ser 20	aga Arg	148
ttc Phe	tgc Cys	cct Pro	cca Pro 25	aga Arg	aag Lys	tct Ser	tgc Cys	cat His 30	gat Asp	tgg Trp	ata Ile	gga Gly	ccc Pro 35	cca Pro	gat Asp	196
aaa Lys	tat Tyr	tca Ser 40	aac Asn	ctt Leu	cga Arg	cct Pro	gtt Val 45	cac His	ttt Phe	tac Tyr	ata Ile	cct Pro 50	gaa Glu	aat Asn	gaa Glu	244
tct Ser	cca Pro 55	ttg Leu	gaa Glu	caa Gln	aag Lys	ctt Leu 60	aga Arg	aaa Lys	tta Leu	aga Arg	caa Gln 65	gaa Glu	aca Thr	caa Gln	gaa Glu	292
Trp 70	Asn	caa Gln	Gln	Phe	Trp 75	Ala	Asn	Gln	Asn	Leu 80	Thr	Phe	Ser	Lys	Glu 85	340
Lys	Glu	gaa Glu	Phe	Ile 90	His	Ser	Arg	Leu	Lys 95	Thr	Lys	Gly	Leu	Gly 100	Leu	388
Arg	Thr	gaa Glu	Ser 105	Gly	Gln	Lys	Ala	Thr 110	Leu	Asn	Ala	Glu	Glu 115	Met	Ala	436
gac Asp	ttc Phe	tac Tyr 120	aag Lys	gaa Glu	ttt Phe	tta Leu	agt Ser 125	aaa Lys	aat Asn	ttt Phe	cag Gln	aag Lys 130	cac His	atg Met	tat Tyr	484
tat Tyr	aac Asn 135	aga Arg	gat Asp	tgg Trp	tac Tyr	aag Lys 140	cgc Arg	aat Asn	ttt Phe	gcc Ala	atc Ile 145	acc Thr	ttc Phe	ttc Phe	atg Met	532
gga Gly 150	aaa Lys	gtg Val	gcc Ala	Leu	gaa Glu 155	agg Arg	att Ile	tgg Trp	aac Asn	aag Lys 160	ctt Leu	aaa Lys	cag Gln	aaa Lys	caa Gln 165	580
aag Lys	aag Lys	agg Arg	agc Ser	aac Asn 170	tagg	gagt	cca (	ctct	gacc	ca go	ccaga	agtc	c agg	gttt		635
aggaagcara tggageteet tteacagggg etetgagaaa aactggaget gateteaaga 695 ageeccacat etteetaagg ggeeccatgg eetgtttggg ggeagggtag gteetgggge 755																

<221> sig\_peptide

actgtgggcc gcctgcctgc tgatgtggg gtgaaataaa gcccaagcac tgggaaaaa	c totaggocag ottgttgtca ogtaogtggt a aaaaaa	815 851
·	•	
<210> 244 <211> 495 <212> DNA <213> Homo sapiens		
<220>		
<221> CDS <222> 89334		
er en		
<221> sig_peptide <222> 89130		
<223> Von Heijne matrix	·	•
score 3.59999990463257 seq AFTLXSLLQAALL/CV		
<221> polyA_signal <222> 462467		
<221> polyA_site <222> 484495		
<400> 244		
agtaggaasg cgccgsccgt ggaggcgcc	a cgtcccttgc sgcggcggga gagamatcgc	60
	atg gcc ttt acc ctg tas tca ctg Met Ala Phe Thr Leu Xaa Ser Leu -10	112
ctg cag gca gcc ctg ctc tgc gtc	aac gcc atc gca gtg ctg cac gag	160
Leu Gln Ala Ala Leu Leu Cys Val	Asn Ala Ile Ala Val Leu His Glu 5 10	
gag cga ttc ctc aag aac att ggc	tgg gga aca gac cag gga att ggt	208
Glu Arg Phe Leu Lys Asn Ile Gly 15	Trp Gly Thr Asp Gln Gly Ile Gly 20 25	
gga ttt gga gaa gag ccg gga att	aaa tca sag sta atg avs ctt att	256
Gly Phe Gly Glu Glu Pro Gly Ile	: Lys Ser Xaa Xaa Met Xaa Leu Ile 35 40	
cga tot gta aga acc gtg atg aga	gtg cca ttg ata ata gta aac tca	304
Arg Ser Val Arg Thr Val Met Arg 45 50	y Val Pro Leu Ile Ile Val Asn Ser 55	
att gca att gtg tta ctt tta tta	ttt gga tgaatwtcat tggagaaaat	354
Ile Ala Ile Val Leu Leu Leu Leu 60 65	n Phe Gly	
ggakactcag aaraggacat gccaktara	aa kttattactt tggtcattat tggaatattt	414
atatettage tggetgaeet tgeaettgt tttetatta aaaaaaaaa a	c aaaaatgtaa agctgaaaat aaaaccaggg	474 495
tttttattta aaaaaaaaaa a		
<210> 245		
<211> 884		
<212> DNA <213> Homo sapiens		
-		
<220> <221> CDS		
<222> 21614		

WO 99/31236 -168-PCT/IB98/02122

<222> 21..835 <223> Von Heijne matrix score 10 seq LWALAMVTRPASA/AP

<221> polyA\_signal <222> 849..854

<221> polyA\_site <222> 873..884

<400> 245									
aataccttag accctcagtc atg cca gtg cct gct ctg tgc ctg ctc tgg gcc 53  Met Pro Val Pro Ala Leu Cys Leu Leu Trp Ala									
		Met P	ro val P 20	ro Ala L	eu Cys L -15	eu Leu Tr	rp Ala		
ctg gca atg	gtg acc	cgg cct	gcc tca	gcg gcc	ccc ata	ggc ggc	cca 101		
Leu Ala Met	Val Thr	Arg Pro	Ala Ser	Ala Ala	Pro Met	Gly Gly	Pro		
gaa ctg gca	cag cat	_	cto acc	ta cta	ttc cat	5	St. 140		
Glu Leu Ala	Gln His	Glu Glu	Leu Thr	Leu Leu	Phe His	Glv Thr	ctg 149 Leu		
	10 .		15			20			
cag ctg ggc	Cag gcc	Ctc aac	ggt gtg	tac agg	acc acg	gag gga	cgg 197		
Gln Leu Gly 25	orn wid	. Ded Abii	30	lyr Arg	Thr Thr	GIn GIA	Arg		
ctg aca aag	gcc agg	aac agc	ctg ggt	ctc tat	aac cac	aca ata	gaa 245		
Leu Thr Lys	Ala Arg	Asn Ser	Leu Gly	Leu Tyr	Gly Arg	Thr Ile	Glu		
ctc ctg ggg	caq qaq	45 gtc agc	caa aac	COO Cat	50		<b>7</b>		
ned hed GIA	Gln Glu	Val Ser	Arg Gly	Arg Asp	Ala Ala	Gln Glu	ctt 293 Leu		
55		60		65			70		
cgg gca agc Arg Ala Ser	Ctg ttg	gaa act	car atg	gag gag	gat att	ctg cas	ctg 341		
	75	Giù IIII	GIN MEC	80	Asp IIe	Leu Xaa 85	Leu		
cag gca rag	gcc aca	gct gag	gtg ctg	aga gag	gtg gcc	cad dca	car 389		
Gln Ala Xaa	Ala Thr	Ala Glu	Val Leu	Gly Glu	Val Ala	Gln Ala	Gln		
aag gtg cta		age gtg	95 Cag cgg	cta daa	kta osa	100	125		
Lys Val Leu	Arg Asp	Ser Val	Gln Arg	Leu Xaa	Xaa Gln	Leu Xaa	asc 437 Xaa		
105			110		115				
gcc tgg ctg	ggc cct	gcc tac	cga aaa	ttt gar	gtc tta	aag gcy	ccc 485		
Ala Trp Leu 120	GIY PIO	125	Arg Lys	Pne Glu	Val Leu 130	Lys Ala	Pro		
cck gam aar	car aac	cac atc	cta tgg	gcc ctc	aca ggc	cac gtg	cak 533		
Pro Xaa Lys 135	Gln Asn	His Ile	Leu Trp	Ala Leu	Thr Gly	His Val	Xaa		
cgg car arg	coo gar	140	aca cad	145			150		
Arg Gln Xaa	Arg Glu	Met Val	Ala Gln	Gln Xaa	Xaa Leu	Cna car	atc 581		
	155			160		165			
cag gar aaa	ctc cac	aca gcg	gcg ctc	cca gcc	tgaatct	gcc tggat	ggaac 634		
Gln Glu Lys	170	ini Ala	Ara Leu 175	Pro Ala					
tgaggaccaa t	catgetge	ca aggaa	cactt cc	acgccccg	tgaggcc	cct gtgca	gggag 694		
gagetgeetg t	cactgg	ga tcagc	caggg cq	ccqqqccc	cacttctc	gag cacag	agear 754		
agacagacgc aggcggggac aaaggcagag gatgtagccc cattggggag gggtggagga aggacatgta ccctttcatr mctacacacc cctcattaaa gcavagtcgt ggcatctcaa									
aaaaaaaaa	······	-r mctaca	acace ce	LCattaaa	gcavagt	cgt ggcat			
							884		

<sup>&</sup>lt;210> 246

<sup>&</sup>lt;211> 897

<sup>&</sup>lt;212> DNA

```
<213> Homo sapiens
  <220>
  <221> CDS
  <222> 94..573
  <221> sig peptide
  <222> 94..258
  <223> Von Heijne matrix
        score 4.69999980926514
        seq IGILCSLLGTVLL/WV
  <221> polyA signal
<222> 862..867
 ' <221> polyA_site
  <222> 886..897
   <400> 246
  aagggcggct gcctagcacc cggaagagcc gtcaacttag cgagcgcaac aggctgccgc
                                                                         60
  tgaggagctg gagctggtgg ggactgggcc gca atg gac aag ctg aag aag gtg
                                                                         114
                                        Met Asp Lys Leu Lys Lys Val
                                        -55
                                                                         162
   ctg agc ggg cag gac acg gag gac cgg agc ggc ctg tec gag gtt gtt
  Leu Ser Gly Gln Asp Thr Glu Asp Arg Ser Gly Leu Ser Glu Val Val
               -45
                                   -40
                                                                         210
   gag gca tct tca tta agc tgg agt acc agg ata aaa ggc ttc att gcg
   Glu Ala Ser Ser Leu Ser Trp Ser Thr Arg Ile Lys Gly Phe Ile Ala
                               -25
           -30
   tgt ttt gct ata gga att ctc tgc tca ctg ctg ggt act gtt ctg ctg
                                                                         258
   Cys Phe Ala Ile Gly Ile Leu Cys Ser Leu Leu Gly Thr Val Leu Leu
                           -10
                                                -5
                                                                         306
   tgg gtg ccc agg aag gga cta cac ctc ttc gca gtg ttt tat acc ttt
   Trp Val Pro Arg Lys Gly Leu His Leu Phe Ala Val Phe Tyr Thr Phe
                   5
                                       10
   ggt aat atc gca tca att ggg agt acc atc ttc ctc atg gga cca gtg
                                                                         354
   Gly Asn Ile Ala Ser Ile Gly Ser Thr Ile Phe Leu Met Gly Pro Val
                                   25
                                                                         402
   aaa cag ctg aag cga atg ttt gag cct act cgt ttg att gca act atc
   Lys Gln Leu Lys Arg Met Phe Glu Pro Thr Arg Leu Ile Ala Thr Ile
                               40
   atg gtg ctg ttg tgt ttt gca ctt acc ctg tgt tct gcc ttt tgg tgg
                                                                         450
   Met Val Leu Cys Phe Ala Leu Thr Leu Cys Ser Ala Phe Trp Trp
                           55
   cat aac aag gga ctt gca ctt atc ttc tgc att ttg cag tct ttg gca
                                                                         498
   His Asn Lys Gly Leu Ala Leu Ile Phe Cys Ile Leu Gln Ser Leu Ala
                                            75
                       70
   ttg acg tgg tac agc ctt tcc ttc ata cca ttt gca agg gat gct gtg
                                                                          546
   Leu Thr Trp Tyr Ser Leu Ser Phe Ile Pro Phe Ala Arg Asp Ala Val
                   85
                                        90
   aaa aad tgt ttt gcc gtg tgt ctt gca taattcatgg ccagttttat
                                                                          593
   Lys Xaa Cys Phe Ala Val Cys Leu Ala
                                                                          653
   gaagetttgg aaggeactat ggacagaage tggtggacag ttttgtwact atettegaaa
   cctctgtctt acagacatgt gccttttatc ttgcagcaat gtgttgcttg tgattcgaac
                                                                          713
   atttgagggt tacttttgga agcaacaata cattctcgaa cctgaatgtc agtagcacag
                                                                          773
    gatgagaagt gggttctgta tcttgtggag tggaatcttc ctcatgtacc tgtttcctct
                                                                          833
    ctggatgttg tcccactgaa ttcccatgaa tacaaaccta ttcagcaaca gcaaaaaaaa
                                                                          893
                                                                          897
    aaaa
```

```
<210> 247
<211> 518
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 74..397
<221> sig_peptide
<222> 74..127
<223> Von Heijne matrix
    score 7.69999980926514
     seq LLLLPVLGLLVSS/KT
<221> polyA signal
<222> 472..477
<221> polyA site
<222> 507..518,
<400> 247
aaagaaagag ctgcsgtgca ggaattcgtg tgccggattt ggttagctga gcccaccgag
                                                                       60
aggegeetge agg atg aaa get ete tgt ete ete ete eet gee etg-
                                                                      109
            . Met Lys Ala Leu Cys Leu Leu Leu Pro Val Leu
                           -15
ggg ctg ttg gtg tct agc aag acc ctg tgc tcc atg gaa gaa gcc atc
                                                                     157
Gly Leu Leu Val Ser Ser Lys Thr Leu Cys Ser Met Glu Glu Ala Ile
                        1
aat gag agg atc cag gag gtc gcc ggc tcc cta ata ttt agg gca ata
                                                                      205
Asn Glu Arg Ile Gln Glu Val Ala Gly Ser Leu Ile Phe Arg Ala Ile
               15
                                    20
age age att gge ega ggg age gag age gte ace tee agg ggg gae etg
                                                                      253
Ser Ser Ile Gly Arg Gly Ser Glu Ser Val Thr Ser Arg Gly Asp Leu
get act tgc ccc cga ggc ttc gcc gtc acc ggc tgc act tgt ggc tcc
                                                                      301
Ala Thr Cys Pro Arg Gly Phe Ala Val Thr Gly Cys Thr Cys Gly Ser
gcc tgt ggc tcg tgg gat gtg cgc gcc gag acc aca tqt cac tqc caq
                                                                      349
Ala Cys Gly Ser Trp Asp Val Arg Ala Glu Thr Thr Cys His Cys Gln
   60
tgc gcg ggc atg gac tgg acc gga gcg cgc tgc tgt cgt gtg cag ccc
                                                                      397
Cys Ala Gly Met Asp Trp Thr Gly Ala Arg Cys Cys Arg Val Gln Pro
                                        85
tgaggtcgcg cgcagcgcgt gcacagcgcg ggcggaggcg gctccaggtc cggaggggtt
                                                                      457
9C999ggagc tggaaataaa cctggagatg atgatgatga tgatqatgqa aaaaaaaaa
                                                                      517
                                                                      518
```

<211> 350

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 51..242

<221> sig\_peptide

<222> 51..116

<223> Von Heijne matrix

score 6.5 seq SCLCPALFPGTSS/FI

<221> polyA\_signal <222> 319..324

<221> polyA site <222> 339..350

<400> 248 56 acgtcattcc anaaccacac ccttgcanag ctttgtactc cgcaccccag atg atc Met Ile tcc agg cag ctc aga tct ctt tcc tgc ctt tgc cct gca ctg ttc ccc 104 Ser Arg Gln Leu Arg Ser Leu Ser Cys Leu Cys Pro Ala Leu Phe Pro -15 -10 ggt act tee tee ttt att gta gea ete age tee eea gee gat etg tae 152 Gly Thr Ser Ser Phe Ile Val Ala Leu Ser Ser Pro Ala Asp Leu Tyr 200 atc cct cav agg cas cga tct gat gaa ttg gtt ttt gaa tcc car aaa Ile Pro Xaa Arg Xaa Arg Ser Asp Glu Leu Val Phe Glu Ser Gln Lys 20 242 ggg tot gcc atg gag ttg gca gtc atc acg gta rat ggc gta Gly Ser Ala Met Glu Leu Ala Val Ile Thr Val Xaa Gly Val 35 302 tqattttgct gaattttaaa taaaatgaaa accataaatt acatratgct tttattgach cttgacmact ggcctaaata aaaaractct gactccaaaa aaaaaaaa 350

<210> 249

<211> 996

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 111..191

<221> sig\_peptide

<222> 111..155

<223> Von Heijne matrix score 5.80000019073486 seq FLXLMTLTTHVHS/SA

<221> polyA signal

<222> 965..970

<221> polyA site

<222> 986..996

<400> 249

60 atcogataca gaacatgcag taatgtggac tgcccaccag aagcaggtga tttccgagct 116 cagcaatgct cagctcataa tgatgtcaag caccatggcc agttttatga atg ggy Met Gly tto otg wgt ota atg acc otg aca acc cat gtt cac toa agt goo aag 164 Phe Leu Xaa Leu Met Thr Leu Thr Thr His Val His Ser Ser Ala Lys -10 cca aat gaa caa ccc tgg ttg ttg aac tagcacctaa ggtcttarat 211 Pro Asn Glu Gln Pro Trp Leu Leu Asn

ggtacgcgtt gctatacaga atctttggat atgtgcatca gtggtttatg ccaaattgtt

WO 99/31236 -172- PCT/IB98/02122

331

ggctgcgatc accagctggg aagcaccgtc aaggaarata actgtggggt ctgcaacrga

natgggtca cctgccggct tcrgatgata ctgtggttgc ggtcctgatc acttatatct ctcasctca caggaacttt gacwdagaga tactgagat actcgggct ccgctgacag tggagggara cggatttctt tcggctgatg gctacgatct tacccagaga acatcaaacc gccaggtcag tcaaatttgc ttatttaaat taaaatgaaa aaaaa	aattccctat ggaggaarccawa acccttgtggac aatggttggacca ctctactgctca gaggaggagcaac cggtaggttgattt gtc	aagtakac atattegecetecagg ggactaavetectagtg tggactecageag atttcatecatectect atcaacceaacctgtg gaggaggetgtgggttg ctgaccaetecaggagt gcaacttecataaaca taactcaggagg	ect tgtcttaaaa 451 wgg tgaaaacagt 511 eca gaawttteca 571 egt caawattegt 631 eat catccacega 691 eta tcagetgaca 751 ata etgtcactat 811 egga teettgteca 871 eggt teeaaatagg 931
			1
<210> 250 <211> 860 <212> DNA <213> Homo sapiens			
<220>			•
<221> CDS		1	
<222> 45602			•
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 45107 &lt;223&gt; Von Heijne matr:</pre>		. *	
<221> polyA_signal <222> 828833			
<221> polyA_site <222> 850860	•	·	
<400> 250 acctetetee aegaggetge	cggcttagga cco		tcg ccc tct 56 Ser Pro Ser
ggt cgc ctg tgt ctt ct Gly Arg Leu Cys Leu Le -15	c acc atc gtt eu Thr Ile Val -10	ggc ctg att ctc Gly Leu Ile Leu -5	CCC acc aga 104
gga cag acg ttg aaa ga Gly Gln Thr Leu Lys As 1 5	at acc acg tcc	agt tot toa goa	gac tca act 152 Asp Ser Thr 15
atc atg gac att cag gt Ile Met Asp Ile Gln Va 20	c ccg aca cga al Pro Thr Arg	gcc cca gat gca Ala Pro Asp Ala 25	gtc tac aca 200
gaa ctc cag ccc acc to Glu Leu Gln Pro Thr Se 35	ct cca acc cca er Pro Thr Pro 40	acc tgg cct gct Thr Trp Pro Ala	gat gaa aca 248
cca caa ccc cag acc ca Pro Gln Pro Gln Thr Gl 50	In Thr Gln Gln 55	Leu Glu Gly Thr 60	gat ggg cct 296 Asp Gly Pro
cta gtg aca gat cca ga Leu Val Thr Asp Pro Gl	lu Thr His Xaa 70	agc mcc aaa gca Ser Xaa Lys Ala 75	Ala His Pro
act gat gac acc acg ac Thr Asp Asp Thr Thr Th 80	ır Leu Ser Glu	aga cca tcc cca	agc aca kac 392 Ser Thr Xaa 95

·	
gtc cat dac aga ccb cba kda ccc tca akc cat ctg gtt ttc atg agg Val His Xaa Arg Pro Xaa Xaa Pro Ser Xaa His Leu Val Phe Met Arg 100 105 110	440
atg acc cct tct tct atg atg aac aca ccc tcc gga aac sgg ggc tgt  Met Thr Pro Ser Ser Met Met Asn Thr Pro Ser Gly Asn Xaa Gly Cys  115 120 125	488
tgg tcg cag ctg tgc tgt tca tca cag gca tca tca tcc tca cca gtg Trp Ser Gln Leu Cys Cys Ser Ser Gln Ala Ser Ser Ser Ser Pro Val	536
gca agt gca ggc agc tgt ccc ggt tat gcc gga atc att gca ggt gag Ala Ser Ala Gly Ser Cys Pro Gly Tyr Ala Gly Ile Ile Ala Gly Glu	584
tcc atc aga aac agg agc tgacaacctg ctgggcaccc gaagaccaag Ser Ile Arg Asn Arg Ser	632
160  ccccctgcca gctcaccgtg cccagcctcc tgcatcccct cgaagagcct ggccagagag ggaagacaca gatgatgaag ctggagccag ggctgccggt ccgagtctcc tacctcccc aaccctgccc gcccctgaag gctacctggc gccttggggg ctgtccctca agttatctcc tctgctaaga caaaaagtaa agcactgtgg tctttgcaaa aaaaaaaa	692 <sup>1</sup> 752 812 860
<210> 251	
<211> 593 <212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	'
<222> 24560	
<221> sig_peptide	
<222> 24101	
<223> Von Heijne matrix	
score 10.3999996185303 seq LLLLLCGPSQDQC/RP	
<221> polyA signal	
<222> 563568	
<221> polyA_site	
<222> 583593	
4400. 251	
<400> 251 aanccagetg esgeeggeea gee atg gag act gga geg etg egg ege eeg caa	53
Met Glu Thr Gly Ala Leu Arg Arg Pro Gln -25 -20	
-25 -20 ctt ctc ccg ttg ctg ctg ctc tgc ggc cct tcc cag gat caa tgc	101
Leu Leu Pro Leu Leu Leu Leu Cys Gly Pro Ser Gln Asp Gln Cys	
-15 -10 -5 cga cct gta ctc cag aat ctg ttg cag agc cca ggc ttg aca tgg agc	149
Arg Pro Val Leu Gln Asn Leu Leu Gln Ser Pro Gly Leu Thr Trp Ser	
1 5 . 10 15	107
ttg gaa gtg ccc act ggg aga gaa gga aag gaa ggt ggg gat cgg gga Leu Glu Val Pro Thr Gly Arg Glu Gly Lys Glu Gly Gly Asp Arg Gly	197
20 25 30	
cca ggg cta akt ggg gcc act cca gcc agg agc cct cag ggc aag gag	245
Pro Gly Leu Xaa Gly Ala Thr Pro Ala Arg Ser Pro Gln Gly Lys Glu	
35 40 45	
35 40 45 atg ggg aga caa agg acc aga aag gtg aag ggc cct gct tgg akt cac	293
	293

WO 99/31236 -174 - PCT/IB98/02122

Thr Ala Asn Glm Glu Leu Asn Arg Met Arg Ser Leu Ser Ser Gly Ser  70 75 80	41
gtg cca gtg ggg cat ctg gag ggt ggc acg gtc aag ctt cag aag gac Val Pro Val Gly His Leu Glu Gly Gly Thr Val Lys Leu Gln Lys Asp 85 90 95	89
acg ggc ctc cat tcc tgc ara gat ggt atg gct tct ctt gaa ggg acg Thr Gly Leu His Ser Cys Xaa Asp Gly Met Ala Ser Leu Glu Gly Thr 100 105 110	37
CCa gct tca gtc ctg gct gat gct tgc cca gga ttc cat gat gtg aan Pro Ala Ser Val Leu Ala Asp Ala Cys Pro Gly Phe His Asp Val Xaa 115 120 125	85
gtt car arg gcc cta ttt ggg tta agt ggg ana rta ctg tgg ctg aaa Val Gln Xaa Ala Leu Phe Gly Leu Ser Gly Xaa Xaa Leu Trp Leu Lys 130 135 140	33
acc cac ttc tgc ctt tct att ana ctt taaataaact ctgaaracct Thr His Phe Cys Leu Ser Ile Xaa Leu 145 150	80
gtaaaaaaa aaa	93
and the control of t The control of the control of	
<210> 252	
<211> 1114	
<212> DNA <213> Homo sapiens	
Table Supreme	
<220> <221> CDS	
<222> 109558	
<221> sig_peptide <222> 109273	
<223> Von Heijne matrix	
score 3.7000004768372 seq VAFMLTLPILVCK/VQ	
score 3.70000004768372	
score 3.7000004768372 seq VAFMLTLPILVCK/VQ <221> polyA_site	
score 3.7000004768372 seq VAFMLTLPILVCK/VQ  <221> polyA_site <222> 11041114  <400> 252 attagctstc caaggtetee eccageactg aggagetege etgetgeeet ettgegegeg	60
score 3.70000004768372 seq VAFMLTLPILVCK/VQ  <221> polyA_site <222> 11041114  <400> 252 attagctstc caaggtctcc cccagcactg aggagctcgc ctgctgccct cttgcgcgcg ggaagcagca ccaagttcac ggccaacgcc ttggcactag ggtccaga atg gct aca Met Ala Thr -55	117
score 3.70000004768372 seq VAFMLTLPILVCK/VQ  <221> polyA_site <222> 11041114  <400> 252 attagctstc caaggtctcc cccagcactg aggagctcgc ctgctgccct cttgcgcgcg ggaagcagca ccaagttcac ggccaacgcc ttggcactag ggtccaga atg gct aca Met Ala Thr -55 aca gtc cct gat ggt tgc cgc aat ggc ctg aaa tcc aag tac tac aga Thr Val Pro Asp Gly Cys Arg Asn Gly Leu Lys Ser Lys Tyr Tyr Arg -50 -45 -40	
score 3.70000004768372 seq VAFMLTLPILVCK/VQ  <221> polyA_site <222> 11041114  <400> 252 attagctstc caaggtctcc cccagcactg aggagctcgc ctgctgccct cttgcgcgcg ggaagcagca ccaagttcac ggccaacgcc ttggcactag ggtccaga atg gct aca Met Ala Thr -55 aca gtc cct gat ggt tgc cgc aat ggc ctg aaa tcc aag tac tac aga Thr Val Pro Asp Gly Cys Arg Asn Gly Leu Lys Ser Lys Tyr Tyr Arg -50 -45 -40	117
score 3.70000004768372 seq VAFMLTLPILVCK/VQ  <221> polyA_site <222> 11041114  <400> 252 attagctstc caaggtetec eccagcactg aggagetege etgetgeeet ettgegegeg ggaagcagca ecaagteac ggecaacgee ttggcactag ggtecaga atg get aca  Met Ala Thr  -55 aca gtc cet gat ggt tge ege aat gge etg aaa tee aag tac tac aga Thr Val Pro Asp Gly Cys Arg Asn Gly Leu Lys Ser Lys Tyr Tyr Arg  -50  -45  ctt tgt gat aag get gaa get tgg gge ate gte eta gaa acg gtg gee Leu Cys Asp Lys Ala Glu Ala Trp Gly Ile Val Leu Glu Thr Val Ala  -35  -30  -25 aca gee ggg gtt gtg ace teg gtg gee tte atg etg act ete eeg ate Thr Ala Gly Val Val Thr Ser Val Ala Phe Met Leu Thr Leu Pro Ile	117 165
score 3.70000004768372 seq VAFMLTLPILVCK/VQ  <221> polyA_site <222> 11041114  <400> 252 attagctstc caaggtetee eccageactg aggagetege etgetgeeet ettgegegeg ggaageagea ecaagtteae ggecaacgee ttggeactag ggtecaga atg get aca Met Ala Thr -55  aca gtc cet gat ggt tge ege aat gge etg aaa tee aag tae tae aga Thr Val Pro Asp Gly Cys Arg Asn Gly Leu Lys Ser Lys Tyr Tyr Arg -50 -45 ctt tgt gat aag get gaa get tgg gge ate gte eta gaa acg gtg gee Leu Cys Asp Lys Ala Glu Ala Trp Gly Ile Val Leu Glu Thr Val Ala -35 -30 -25 aca gee ggg gtt gtg ace teg gtg gee tte atg etg act ete eeg ate Thr Ala Gly Val Val Thr Ser Val Ala Phe Met Leu Thr Leu Pro Ile -20 -15 -10 -5 cte gte tge aag gtg cag gae tee ase agg ega aaa atg etg eet act Leu Val Cys Lys Val Gln Asp Ser Asn Arg Arg Lys Met Leu Pro Thr	117 165 213
score 3.70000004768372 seq VAFMLTLPILVCK/VQ  <221> polyA_site <222> 11041114  <400> 252 attagctstc caaggtctcc cccagcactg aggagctcgc ctgctgccct cttgcgcgcg ggaagcagca ccaagttcac ggccaacgcc ttggcactag ggtccaga atg gct aca	117 165 213 261
score 3.70000004768372 seq VAFMLTLPILVCK/VQ  <221> polyA_site <222> 11041114  <400> 252 attagctstc caaggtctcc cccagcactg aggagctcgc ctgctgccct cttgcggcgg ggaagcagca ccaagttcac ggccaacgcc ttggcactag ggtccaga atg gct aca	117 165 213 261 309
score 3.70000004768372 seq VAFMLTLPILVCK/VQ  <221> polyA_site <222> 11041114  <400> 252 attagctstc caaggtctcc cccagcactg aggagctcgc ctgctgccct cttgcgcgcg ggaagcagca ccaagttcac ggccaacgcc ttggcactag ggtccaga atg gct aca	117 165 213 261 309

30 35 40	:
ctc ttt ggg atc ctc ttt tcc atc tgc ttc tcc tgc ctg ctg gct cat. Leu Phe Gly Ile Leu Phe Ser Ile Cys Phe Ser Cys Leu Leu Ala His 45 50 55 60	453
gct gtc agt ctg acc aag ctc gtc cgg ggg agg aaa gcc cct ttc cct Ala Val Ser Leu Thr Lys Leu Val Arg Gly Arg Lys Ala Pro Phe Pro	501
65 70 75 gtt ggt gat tct ggg tct ggc cgt ggg ctt cag cct agt cca gga tgt Val Gly Asp Ser Gly Ser Gly Arg Gly Leu Gln Pro Ser Pro Gly Cys 80 85 90	549
tat cgc tat tgaatatatt gtcctgacca tgaataggac caacgtcaat Tyr Arg Tyr 95	598
gtctttctg agctttccgc tcctcgtcgc aatgaaaact ttgtcctcct gctcacctac ktcctcttct tgatggcgct gaccttcctc wtgtcctcct tcaccttctg tggtkccttc acgggctgga avagacatgg ggcccacatc tacctcasga tgctcskctc cattgccatc tgggtggcct ggatcaccct gctcatgctt cctgactttg accgcrggtg ggatgacacc atcmtcarct ccgccttggs trcsaatggc tgggtgttcc tgttggctta tgttagtccc gagttttggc tgctcacaaa gcaackaaac cccatggatt atcctgttga ggatgcttct tgtaaacctc aactcgtgaa gaagagctat ggtgtggrga acagagccta skctcaagag gaaatcactc aaggttttga agagacaggg gacacgctct atgccccta ttccacacat ttccagctgc agaascagcc tccccaaaaa aaaaaa	658 718 778: 838 898 958 1018 1078
<210> 253 <211> 1182	
<212> DNA <213> Homo sapiens	÷
<220> <221> CDS <222> 128835	
<221> sig_peptide <222> 128220 <223> Von Heijne matrix score 4.69999980926514 seq LAVDSWWLDPGHA/AV	:
<221> polyA_signal <222> 11451150	
<221> polyA_site <222> 11701181	
<pre>&lt;400&gt; 253 aagaactgcg tctcgcgacc caggcgcggg ttcccggagg acagccaaca agcgatgctg ccgccgccgt ttcctgattg gttgtgggtg gctacctctt cgttctgatt ggccgctagt gagcaag atg ctg agc aag ggt ctg aag cgg aaa cgg gag gag gag Met Leu Ser Lys Gly Leu Lys Arg Lys Arg Glu Glu Glu -30 -25 -20</pre>	60 120 169
gag aag gaa cct ctg gca gtc gac tcc tgg tgg cta gat cct ggc cac Glu Lys Glu Pro Leu Ala Val Asp Ser Trp Trp Leu Asp Pro Gly His -15 -10 -5	217
gca gcg gtg gca cag gca ccc ccg gcc gtg gcc tct agc tcc ctc ttt Ala Ala Val Ala Gln Ala Pro Pro Ala Val Ala Ser Ser Ser Leu Phe  1 5 10 15	265
gac ctc tca gtg ctc aag ctc cac cac agc ctg cag vrr agt rag ccg Asp Leu Ser Val Leu Lys Leu His His Ser Leu Gln Xaa Ser Xaa Pro 20 25 30	313
gac ctg cgg cac ctg gtg ctg gtc atr aac act ctg cgg cgc atc cag	361

Asp	Leu	Arg	His 35	Leu	Val	Leu	Val	Xaa 40	Asn	Thr	Leu	Arg	Arg 45	Ile	Gln	
							gcc Ala 55									409
		ccc					aac Asn									457
	tca						ctc Leu									505
					ccc Pro		ccc Pro			gac						553
_	_	Ile		gga	wca	_	ccc Pro		ctg		_	_				601
		gcc	act				ctg Leu 135	gac								649
	_	att	_			_	tat Tyr	_		_		tgg				697
	gag					ggc	cct Pro				ccg			-	_	745
gct					gag		gaa Glu			tac Tyr						793
			_	gca	_		cga Arg		ccg	999						835
_	_	-	tgct			_		t at	_		_		tgg		accaac	
															actttg tggcag	
															aattcc	
															aatcag	
							ggaa									1182

<211> 1073

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 59..505

<221> sig\_peptide

<222> 59..358

<223> Von Heijne matrix
 score 3.70000004768372
 seq LASSFLFTMGGLG/FI

<221> polyA\_signal

<222> 1042..1047

<221> polyA\_site

<222> 1062..1073

<400> 254	
actgtttnng ggaggegegt ggggettgag gecgagaacg gecettgetg ccaccaac	58
atg gag act ttg tac cgt gtc ccg ttc tta gtg ctc gaa tgt ccc aac	106
Met Glu Thr Leu Tyr Arg Val Pro Phe Leu Val Leu Glu Cys Pro Asn	
-100 -95 -90 -85	154
ctg aag ctg aag aag ccg ccc tgg ttg cac atg ccg tcg gcc atg act	154
Leu Lys Leu Lys Lys Pro Pro Trp Leu His Met Pro Ser Ala Met Thr	
-80 -75 -70	202
gtg tat gct ctg gtg gtg gtg tct tac ttc ctc atc acc gga gga ata	202
Val Tyr Ala Leu Val Val Ser Tyr Phe Leu Ile Thr Gly Gly Ile -65 -60 -55	
att tat gat gtt att gtt gaa cct cca agt gtc ggt tct atg act gat	250
Ile Tyr Asp Val Ile Val Glu Pro Pro Ser Val Gly Ser Met Thr Asp	
-50 -45 -40	
gaa cat ggg cat cag agg cca gta gct ttc ttg gcc tac aga gta aat .	298
Glu His Gly His Gln Arg Pro Val Ala Phe Leu Ala Tyr Arg Val Asn	
-35 -30 -25	
gga caa tat att atg gaa gga ctt gca tcc agc ttc cta ttt aca atg	346
Gly Gln Tyr Ile Met Glu Gly Leu Ala Ser Ser Phe Leu Phe Thr Met	•
-20 -15 -10 -5	
gga ggt tta ggt ttc ata atc ctg gac gga tcg aat gca cca aat atc	394
Gly Gly Leu Gly Phe Ile Ile Leu Asp Gly Ser Asn Ala Pro Asn Ile	•
1 5 10	
cca aaa ctc aat aga ttc ctt ctt ctg ttc att gga ttc gtc tgt gtc	442
Pro Lys Leu Asn Arg Phe Leu Leu Phe Ile Gly Phe Val Cys Val	
15 20 25	490
cta twr agt ttt tkc ayg gct aga gta ttc atg aga atg aaa ctg ccg	430
Leu Xaa Ser Phe Xaa Xaa Ala Arg Val Phe Met Arg Met Lys Leu Pro	•
30 35 40 ggc tat ctg atg ggt tagagtgcct ttgasaagaa atcagtggat actggatttg	545
Gly Tyr Leu Met Gly	0.0
45	
ctcctgtcaa wgaastttta aaggctgtmc caatcctcta atatgaaatg tggaaaagaa	605
tgaagagcag cagtaaaaga aatatctagt gaaaaaacag gaagcgtatt gaagcttgga	665
ctagaatttc ttcttggtat taaagagaca agtttatcac agaatttttt ttcctgctgg	725
cctattgcta taccaatgat gttgagtggc attttctttt tagtttttca ttaaaatata	785
ttccatatct acaactataa tatcaaataa agtgattatt ttttacaacc ctcttaacat	845
tttttggaga tgacatttct gattttcaga aattaacata aaatccagaa gcaagattcc	905
gtaagctgag aactctggac agttgatcag ctttacctat ggtgctttgc ctttaactag	965
agtgtgtgat ggtagattat ttcagatatg tatgtaaaac tgtttcctga acaataagat	1025
gtatgaacgg agcagaaata aatacttttt ctaattaaaa aaaaaaaa	1073

<211> 818

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 1..207

<221> sig\_peptide

<222> 1..147

<223> Von Heijne matrix score 7.59999990463257 seq HLPFLLLLSCVGX/XP

<221> polyA\_signal <222> 784..789

<221> polyA\_site <222> 807..818 ° <400> 255 48 atg cct ttc cat ttt ccg ttc ctt ggg ttt gtg tgt ctg cat ctc cat Met Pro Phe His Phe Pro Phe Leu Gly Phe Val Cys Leu His Leu His -45 -40 96 ctt acc cct tgc ctg act gta ccc cgt aga ccc ctg ttt ctc ctc ctg Leu Thr Pro Cys Leu Thr Val Pro Arg Pro Leu Phe Leu Leu Leu -30 -25 -20 cac etg tgt ecc cat etg ecc tte ttg ttg etc etg tea tgt gte ggg 144 His Leu Cys Pro His Leu Pro Phe Leu Leu Leu Ser Cys Val Gly -15 -10 -5 gke www ecc tee tgt etg ect tet tee tee act tgt gte age ttg eat 192 Xaa Xaa Pro Ser Cys Leu Pro Ser Ser Ser Thr Cys Val Ser Leu His 10 247 ttt ttt att eet gae tgagteacea caccectete ceetgateaa agggaatatk Phe Phe Ile Pro Asp 20 artttttaat ttggatcgac tgaggtgcca ggagaaactg cagkcccagg tatccmvaca 307 gccaccagga tggtccctcg ccccacccc accgcctctk ccccaccttt tccaacgtgt 367 tgcatgctgg gaactggggg gtgtggggga aggggctgcc ggcttctttc aggangctga 427 487 rgtttggarg caaaatcaac ctgggaracc acccggccg cggcgcctca gtggacaggt gggargaaaa gaaaacttct taccttggar garggacatc ccgcttcctt atccttagct 547 607 tttttgttgc tcctccccac tgcccctttt aatttatttg gttgtttgcg gaaggagggg 667 ggaagggggt aagctgggcc gggaactgtc cgaggtgctg agctggggcg ggaccggaat 727 cctcccggta gggtaccagg gactgagttg ggcctggggc cgtgtccaag gtgccaatga 787 tgcgggccga cagarcgggc cgcactgtct gtctgtccgt ctgtcccgga aagaactata 818 aagcgctgga agcgcctgca aaaaaaaaaa a <210> 256 <211> 971 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 12..734 <221> sig\_peptide <222> 12..101 <223> Von Heijne matrix score 4.80000019073486 seq ILFCVGAVGACTL/SV <221> polyA signal <222> 914..919 <221> polyA\_site <222> 961..971 <400> 256 aatacacaga a atg ggg act gcg agc aga agc aac atc gct cgc cat ctg 50 Met Gly Thr Ala Ser Arg Ser Asn Ile Ala Arg His Leu -25 98 caa acc aat ctc att cta ttt tgt gtc ggt gct gtg ggc gcc tgt act Gln Thr Asn Leu Ile Leu Phe Cys Val Gly Ala Val Gly Ala Cys Thr -10 146 ctc tct gtc aca caa ccg tgg tac cta gaa gtg gac tac act cat gag

Leu Ser Val Thr Gln Pro Trp Tyr Leu Glu Val Asp Tyr Thr His Glu

	1				5					10					15	
qcc	qtc	acc	ata	aag	tgt	acc	ttc	tcc	gca	acc	gga	tgc	cct	tct	gag	194
		Thr														•
				20					25					30		
caa	cca	aca	tgc	ctg	tgg	ttt	cgc	tac	ggt	gct	cac	cag	cct	gag	aac	242
${\tt Gln}$	Pro	Thr	Cys	Leu	Trp	Phe	Arg	Tyr	Gly	Ala	His	Gln	Pro	Glu	Asn	
			35					40					45			
		ttg														290
Leu	Cys	Leu	Asp	Gly	Cys	Lys		Glu	Ala	Xaa	Lys		Thr	Val	Arg	. •
		50					55					60				
		ctc														338
Glu		Leu	Lys	Glu	Asn		Val	Ser	Leu	Thr		Asn	Arg	Val	Thr	
	65		as .			70					75					306
		gac														386
	Asn	Asp	ser	Ala		ıyr	TIE	Cys	GIA		AIA	Pne	Pro	ser	95	
80					85					90						424
		gcg														434
Pro	GIU	Ala	Arg		гÀг	GIN	THE	GIA	105	GIA	Inr	Inr	Leu	110	val	
	~~~	att	224	100	ata	200	226	~~~			200	++-	ctc		act	482
		Ile														402
Arg	GIU	TIE	115	ьеu	Den	261	пуs	120	neu	Arg	SEI	PIIC	125	TILL	AIG	
a++	~+-	tca		ata	tot	ata	+=+		200	aat	ata	tac		acc	ttc	530
	_	Ser	_			-					_		-			330
Deu	VOI	130	neu	Deu	361	Val	135	V CA 1	¥ 111	Gry	VOI	140	vai	niu	7110	
ata	ctc	ctc	tee	222	tca	aaa		aac	cct	cta	aga	-	aaa	gaa	ata	578
		Leu									_			-		
	145			-,-		150					155		-1-			
aaa	qaa	gac	tca	caa	aaq	aaq	aaq	agt	gct	cgq	cqt	att	ttt	cag	gaa	626
		Asp														
160		-			165	•	-			170	_				175	
att	gct	caa	gaa	cta	tac	cat	aag	aga	cat	gtg	gaa	aca	aat	cag	caa	674
		Gln														
				180					185					190		
tct	gag	aaa	gat	aac	aac	act	tat	gaa	aac	aga	aga	gta	ctt	tcc	aac	722
Ser	Glu	Lys	Asp	Asn	Asn	Thr	Tyr	Glu	Asn	Arg	Arg	Val	Leu	Ser	Asn	
			195					200					205			
tat	gaa	agg	cca	taga	aaac	gtt 1	ttaat	tttt	ca a	tgaag	gtca	c tg	aaaa	tcca		774
Tyr	Glu	Arg	Pro													•
		210														
					_		_								aataaa	834
															tataac	894
taa	takt	cat 1	tacca	aaaat	ta ci	taaa	accc	a ac	aaaa	tgca	act	gaaa	aat	acct	tccaaa	954
ttt	gcca	aaa a	aaaa	aaw												971

 $\tau = 11$ 

<211> 640

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 378..518

<221> sig\_peptide

<222> 378..467

<223> Von Heijne matrix score 5.5 seq SLMTCTTLINASA/IS <221> polyA\_signal <222> 607..612 <221> polyA site <222> 628..640 <400> 257 agoctgggta akqcccaaqa tqqctqtctt cqccttaqta ctcgtqtqaa gttggcgqqq 60 acggttcctg tcatcttctt gggcttattt ggtgtgctgt tgaagggggg agactagaga 120 aatggcaggg aacctottat coggggcagg taggcgcotg tgggactggg tgcctotggc 180 gtgcagaagc ttctctcttg gtgtgcctag attgatcggt ataaggctca ctctcccgcc 240 ccccaaagtg gttgatcgtt ggaacgagaa aagggccatg ttcggagtgt atgacaacat 300 cgggatcctg ggaaactttg aaaagcaccc caaagaactg atcagggggc ccatatggct 360 tcgaggttgg aaaggga atg aat tgc aac gtt gta tcc gaa aga gga aaa 410 Met Asn Cys Asn Val Val Ser Glu Arg Gly Lys : -30 -25 -20 tgg ttg gaa gta gaa tgt tcg ctg atg acc tgc aca acc tta ata aac 458 Trp Leu Glu Val Glu Cys Ser Leu Met Thr Cys Thr Thr Leu Ile Asn -10 -15 gca tcc gct atc tct aca aac act tta acc gac atg gga agt ttc gat 506 Ala Ser Ala Ile Ser Thr Asn Thr Leu Thr Asp Met Gly Ser Phe Asp 558 aga aga gaa agc tgagaacttc ggaaaaggct catctgtcac cctggaraag Arg Arg Glu Ser ggaaactgta cttttccctg tgaggaaacg gctttgtatt ttctctgtaa taaaatgggg 618 cttctttgga aaaaaaaaa aa 640 <210> 258 <211> 745 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 110..304 <221> sig\_peptide <222> 110..193 <223> Von Heijne matrix score 4.59999990463257 seq PLQWSLLVAVVAG/SV <221> polyA signal <222> 708..713 <221> polyA site <222> 732..743 <400> 258 actteegeet gegeetgege ageveagete eshgageeet gecaaceatg gtgaacttgg 60 gtctgtcccg ggtggacgac gccgtggctg ccaagcaccc ggcaccggc atg gcc ttt 118 ggc ttg cag atg ttc att cag agg aag ttt cca tac cct ttg cag tgg 166 Gly Leu Gln Met Phe Ile Gln Arg Lys Phe Pro Tyr Pro Leu Gln Trp -25 -10 -20 -15 age etc eta gtg gee gtg gtt gea gge tet gtg gte age tae ggg gtg 214 Ser Leu Leu Val Ala Val Val Ala Gly Ser Val Val Ser Tyr Gly Val

acg aga gtg gag tcg gag aaa tgc aac aac ctc tgg ctc ttc ctg gag

Thr Arg Val Glu Ser Glu Lys Cys Asn Asn Leu Trp Leu Phe Leu Glu 10 15 20	.·
acc gga cag ctc ccc aaa gac agg agc aca gat cag ara agc Thr Gly Gln Leu Pro Lys Asp Arg Ser Thr Asp Gln Xaa Ser 25 30 35	304
taggagaget ccagcagggg cacagargat tgggggcagg argartetgg aacacakeet teatgeece tgaceceagg cegacetee ecacaceeta gggtaeceea gtegtateet etgteegeat gtgtggecag geetgacaaa emeetgeaga tggetgetge eceaacetgg gacetgecea ggaggttgga geagaaaggg etetecetgg ggtggtgttt eteetetagg gtattgggat geatgttetg cactgecage agaagagggtg tgtetggggg ecaceaceta tgggacaegg ggtegaaggg geetgtaeae tetgteattt eetttetage ecetgeatet ecaacaagte eaaggtgaea getggtgeta ggggggtggg gttaataaat ggettateet tetetecaaa araaaaaaam e	364 424 484 544 604 664 724
<pre>&lt;210&gt; 259</pre>	·
<211> 637	
<212> DNA <213> Homo sapiens	
<220>	
<221> CDS <222> 201419	
<221> sig_peptide <222> 201272	
<223> Von Heijne matrix	
score 6.4000009536743 seq LSYLPLWLGPIWP/CS	•
<221> polyA_signal	
<221> polyA_site <222> 627637	٠
<400> 259	60
acaaaatata attgcctcts ccctctccca ttttctctct tgggagcaat ggtcacagtc cctggtacct gaaaaggtac ctaggtctag gcccttcttc cctttccctt cctctccct	120
accccagaac tttggctccc tttcccttct ctctctggta gctccaggag gcctgtgatc	180 233
cagctccctg cctagcatcc atg acc tgt tgg atg tta cct cca atc agt ttc  Met Thr Cys Trp Met Leu Pro Pro Ile Ser Phe -20 -15	233
ctg tcc tac ctg cct ctt tgg ctt gga cct ata tgg cca tgc tct ggc Leu Ser Tyr Leu Pro Leu Trp Leu Gly Pro Ile Trp Pro Cys Ser Gly -10 -5 1	281
tot acc ctt ggg aag cot gat coc ggt gtg tgg coc agc ttg ttc agg	329
Ser Thr Leu Gly Lys Pro Asp Pro Gly Val Trp Pro Ser Leu Phe Arg 5 10 15	
ccc tgg gat gct gca tct cca ggc aac tat gca ctt tcc cgg gga rar Pro Trp Asp Ala Ala Ser Pro Gly Asn Tyr Ala Leu Ser Arg Gly Xaa	377
20 25 30 35	
aac cak tat gav aak tgg ggg cag ggc aca cat tca tct ttg Asn Xaa Tyr Xaa Xaa Trp Gly Gln Gly Thr His Ser Ser Leu 40	419
targaaggto tggcctgggg terggtgaag gagggcccag gtcagttctg gggtcccagt	479
gacctgcttt gccattctcc tggtgccgct gctgctccct gtttctggag ctggatgttc cccacctggc agttgagctg cctgagccaa tgtgtctgtc tttggtaact gagtgaacca	539 599
taataaaggg gaacatttgg ccctgtgaaa aaaaaaaa	637

```
<210> 260
<211> 1315
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 123..302
<221> sig_peptide
<222> 123..176
<223> Von Heijne matrix
      score 4.30000019073486
      seq WTCLKSFPSPTSS/HA
<221> polyA signal
<222> 1279..1284
<221> polyA site
<222> 1301..1312
<400> 260
aagagcatcc tgcgccccgg cgcggggccc tgcggtagcc tcaggcccct cccctggacc
                                                                     60
cgccgcagag ccagtgcaga atacagaaac tgcagccatg accacgcacg tcaccctgga
                                                                    120
                                                                    167
ag atg ccc tgt cca acg tgg acc tgc ttg aag agc ttc ccc tcc ccg
   Met Pro Cys Pro Thr Trp Thr Cys Leu Lys Ser Phe Pro Ser Pro
               -15
                                  -10
                                                                    215
acc agc agc cat gca tcg agc ctc cac ctt cct cca tca tgt acc agg
Thr Ser Ser His Ala Ser Ser Leu His Leu Pro Pro Ser Cys Thr Arg
            1
cta act ttg aca caa act ttg agg aca gga atg cat ttg tca cgg gca
                                                                     263
Leu Thr Leu Thr Gln Thr Leu Arg Thr Gly Met His Leu Ser Arg Ala
                        20
ttg caa ggt aca ttg acc agg cta cag tcc act cca gca tgaatgarat
Leu Gln Gly Thr Leu Thr Arg Leu Gln Ser Thr Pro Ala
30
gctggaggaa ggacatgakt atgcggtcat gctgtacacc tggcgcagct gttcccgggc
                                                                     372
                                                                     432
cattccccag gtgaaatgca acragcagcc caaccgakta raratctatg araaracagt
araggtgctg gagccggagg tcaccaagct catgaagttc atgtattttc arcgcaaggc
                                                                     492
                                                                     552
catcgagcgg ttctgcascg aggtgaagcg gctgtgccat gccgagcgca ggaaggactt
                                                                     612
tgtctctgag gcctacctcc tgacccttgg caagttcatc aacatgtttg ctgtcctgga
                                                                     672
tgagctaaag aacatgaast gcagcgtcaa raatgaccac tctgcctaca agagggcagc
acagttcctg cggaagatgg cagatcccca gtctatccag gagtcgcaga acctttccat
                                                                     732
gttcctggcc aaccacaaca ggatcaccca gtgtctccac cagcaacttg aagtgatccc
                                                                     792
aggetatgag gagetgetgg etgacattgt caacatetgt gtggattact acgagaacaa
                                                                     852
                                                                     912
gatgtacctg actoccagtg agaaacatat gctcctcaag gtaaaactcc cctgaggccg
cacccatgga gcctgggctt accctctcac cttcttctta ttaaaaaatcc gttttaaaaa
                                                                     972
acaatgtttc tttttctta aacattgata cagatcttac ggcacataat ggtttgtaac
                                                                    1032
ctgttccttt cctgtaatat aatataccgt agtcaccttt ccagatgtca ttaaggctat
                                                                    1092
                                                                    1152
ttctacaatg ttatgtgtaa tgactgccaa gtattctgtt gtattggaac attgtcatgt
aacatatccc ctgtggttgg atatttgcta aacttcattg aacacccttg tagcagtttt
                                                                    1212
                                                                    1272
 tgtgcacatc tttttgtcaa ggcaaacttc ctagaagaga aattgctggc tcaaagggaa
                                                                    1315
```

<sup>&</sup>lt;210> 261

<sup>&</sup>lt;211> 1035

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Homma sapiens

WO 99/31236 -183 - PCT/IB98/02122

<220>

<221> CDS <222> 98..673 ' <221> sig\_peptide <222> 98..376 <223> Von Heijne matrix score 5.59999990463257 seq VLLLRQLFAQAEK/WY <221> polyA\_site <222> 1025..1035 ·<400> 261 60 aattttcygt ggtccaacta ccctcggcga tcccaggctt ggcggggcac cgcctggcct ctcccgttcc tttaggctgc cgccgctgcc tgccgcc atg gca gag ttg ggc cta 115 . Met Ala Glu Leu Gly Leu aat gag cac cat caa aat gaa gtt att aat tat atg cgt ttt gct cgt . 163 Asn Glu His His Gln Asn Glu Val Ile Asn Tyr Met Arg Phe Ala Arg -80 -75 tca aag aga ggc ttg aga ctc aaa act gta gat tcc tgc ttc caa gac 211 Ser Lys Arg Gly Leu Arg Leu Lys Thr Val Asp Ser Cys Phe Gln Asp -65 -70 ctc aag gag agc agg ctg gtg gag gac acc ttc acc ata gat gaa gtc 259 Leu Lys Glu Ser Arg Leu Val Glu Asp Thr Phe Thr Ile Asp Glu Val -50 -45 tct gaa gtc ctc aat gga tta caa gct gtg gtt cat agt gag gtg gaa 307 Ser Glu Val Leu Asn Gly Leu Gln Ala Val Val His Ser Glu Val Glu -35 -30 355 tot gag oto ato aac act goo tat acc aat gtg tta ott otg oga cag Ser Glu Leu Ile Asn Thr Ala Tyr Thr Asn Val Leu Leu Leu Arg Gln -15 403 ctg ttt gca caa gct gag aag tgg tat ctt aag cta cag aca gac atc Leu Phe Ala Gln Ala Glu Lys Trp Tyr Leu Lys Leu Gln Thr Asp Ile 451 tot gaa ott gaa aac oga gaa tta tta gaa caa ktt goa gaa ttt gaa Ser Glu Leu Glu Asn Arg Glu Leu Leu Glu Gln Xaa Ala Glu Phe Glu 15 20 499 aaa gca rav att aca tot toa aac aaa aag coc atc tta dat gto aca Lys Ala Xaa Ile Thr Ser Ser Asn Lys Lys Pro Ile Leu Xaa Val Thr 35 aas cca aaa ctt gct cca ctt aat gaa ggt gga aca gca aaa ctc cta 547 Xaa Pro Lys Leu Ala Pro Leu Asn Glu Gly Gly Thr Ala Lys Leu Leu 45 55 aac aag gta ata tgt att att ttg aga aac gga aag tct ctc att ctg 595 Asn Lys Val Ile Cys Ile Ile Leu Arg Asn Gly Lys Ser Leu Ile Leu tcc tgt cat tgc cta ggg tgg aga aac aaa agt gga agg ttt gtt tca 643 Ser Cys His Cys Leu Gly Trp Arg Asn Lys Ser Gly Arg Phe Val Ser 80 ggt cct ctg agg ata att agt cca ttg cag tagttttact tgatggtacc 693 Gly Pro Leu Arg Ile Ile Ser Pro Leu Gln 95 753 ccatgggcca gaagaggca tacttaacct tctagagagc ctgaagtagc tcctgatcac accttttcaa ggtaaagtga agagcatgaa attttggaca gcgtttattg atggacattt 813 873 aattagccgg gtgtggtggt acgtgcctat agtcagagct actcgggagg ctgaggcagg 933 agaattgctt gaacccggga ggtggaggtt gcagtgagct gagatcacgc cactgcactc 993 tagcctgggc gacagagcga gactccatct caaaaaaaaa aa 1035

```
<210> 262
<211> 696
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 17..463
<221> sig_peptide
<222> 17..232
<223> Von Heijne matrix
      score 3.79999995231628
      seq LMGLALAVYKCQS/MG
<221> polyA_signal
<222> 657..662
<221> polyA_site
<222> 684..696
<400> 262
                                                                       52
acteaaacag attece atg aat etc tte ate atg tae atg gea gge aat act
              Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr
                          -70
                                          1
                                                                      100
atc tcc atc ttc cct act atg atg gtg tgt atg atg gcc tgg cga ccc
Ile Ser Ile Phe Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro
-60
                    -55
                                         -50
att cag gca ctt atg gcc att tca gcc act ttc aag atg tta gaa agt
                                                                      148
Ile Gln Ala Leu Met Ala Ile Ser Ala Thr Phe Lys Met Leu Glu Ser
                                     -35
                -40
tca agc cag aag ttt ctt cag ggt ttg gtc tat ctc att ggg aac ctg
                                                                      196
Ser Ser Gln Lys Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu
                                                     -15
            -25
                                 -20
atg ggt ttg gca ttg gct gtt tac aag tgc cag tcc atg gga ctg tta
                                                                       244
Met Gly Leu Ala Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu
                            -5
cct aca cat gca tcg gat tgg tta gcc ttc att gag ccc cct gag aga
                                                                       292
Pro Thr His Ala Ser Asp Trp Leu Ala Phe Ile Glu Pro Pro Glu Arg
                    10
atg gag tca gtg gtg gag gac tgc ttt tgt gaa cat gag aaa gca gcg
                                                                       340
Met Glu Ser Val Val Glu Asp Cys Phe Cys Glu His Glu Lys Ala Ala
                                     30
cct ggt ccc tat gta ttt ggg tct tat tta cat cct tct tta agc cca
                                                                       388
Pro Gly Pro Tyr Val Phe Gly Ser Tyr Leu His Pro Ser Leu Ser Pro
                                 45
gtg gct cct cag cat act ctt aaa cta atc act tat gtt aaa aaa aac
                                                                       436
Val Ala Pro Gln His Thr Leu Lys Leu Ile Thr Tyr Val Lys Lys Asn
                             60
caa aaa act ctt ttc tcc atg gtg ggg tgacaggtcc taaaaaggaca
                                                                       483
Gln Lys Thr Leu Phe Ser Met Val Gly
                         75
atgtgcatat tacgacaaac acaaaaaaac tataccataa cccagggctg aaaataatgt
                                                                       543
aaaaaacttt atttttgttt ccagtacaga gcaaaacaac aacaaaaaaa cataactatg
                                                                       603
                                                                       663
taaacaaaaa aataactgct gctaaatcaa aaactgttgc agcatctcct ttcaataaat
                                                                       696
taaatggttg araacaatgc aaaaaaaaaa aaa
```

```
<212> DNA
 <213> Homo sapiens
 <220>
 <221> CDS
 <222> 263..481
 <221> sig peptide
 <222> 263..322
 <223> Von Heijne matrix
       score 11.1999998092651
       seg ILVVLMGLPLAQA/LD
 <221> polyA_site
 <222> 858..868
 <400> 263
 aagacacgcc tacgattaga ctcaggcagg cacctaccgg cgagcggccg crvgtgactc
                                                                        60
 ccaggcgcgg cggtacctca cggtggtgaa ggtcacaggg ttgcagcact cccagtagac 120
 caggagetee gggaggeagg geeggeeeca egteetetge geaceaceet gagttggate
                                                                       180
 ctctgtgcgc cacccctgag ttggatccag ggctagctgc tgttgacctc cccactccca
                                                                       240
 egetgeeete etgeetgeag ee atg acg eee etg etc ace etg ate etg gtg
                                                                       292
                           Met Thr Pro Leu Leu Thr Leu Ile Leu Val
                                               -15
                           -20
 gtc ctc atg ggc tta cct ctg gcc cag gcc ttg gac tgc cac gtg tgt
                                                                        340
 Val Leu Met Gly Leu Pro Leu Ala Gln Ala Leu Asp Cys His Val Cys
                      ~5
  -10
  gec tac aac gga gac aac tgc ttc aac ccc atg cgc tgc ccg gct atg
                                                                        388
  Ala Tyr Asn Gly Asp Asn Cys Phe Asn Pro Met Arg Cys Pro Ala Met
                                  15
              10
  gtt gcc tac tgc atg acc acg cgc acc tac tac acc ccc acc agg atg
                                                                        436
  Val Ala Tyr Cys Met Thr Thr Arg Thr Tyr Tyr Thr Pro Thr Arg Met
                              30
          25
                                                                        481
  aag gtc agt aag tcc tgc gtg ccc cgc tgc ttc gar nac tgt gta
  Lys Val Ser Lys Ser Cys Val Pro Arg Cys Phe Glu Xaa Cys Val
  tgatggctac tccaagcacg cgtccaccac ctcctgctgc cagtacgacc tctgcaacgg
  caccggcctt gccaccccgg ccaccctggc cctggccccc atcctcctgg ccaccctctg
                                                                        601
  gggtctcctc taaagccccc gaggcagacc cactcaagaa caaagctctc gagacacact
                                                                        661
  gctayaccet ckcacccake teaccetgee teacceteea cactecetge gaccteetea
                                                                        721
  gecatgecca gggtcaggae tgtgggcaag aagacaceeg aceteeeca aceaccacac
                                                                        781
  gacctcactt cgaggccttg acctttcgat gctgtgtggg atcccaaaag tgtccggctt
                                                                        841
                                                                        868
  tgatgggctg atcagcaaaa aaaaaaa
```

<210> 264
<211> 775
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 42..299

<221> sig\_peptide
<222> 42..101
<223> Von Heijne mata

<223> Von Heijne matrix
 score 5.40000009536743
 seq WFVHSSALGLVLA/PP

<221> polyA\_site

<222> 762..775\n

-10

<400> 264	
aacgatacaa atggtaggcc ttcatgtgag ccagtdacta c atg aat ctt cat ttc Met Asn Leu His Phe -20	56
cca cag tgg ttt gtt cat tca tca gcg tta ggc ttg gtc ctg gct cca Pro Gln Trp Phe Val His Ser Ser Ala Leu Gly Leu Val Leu Ala Pro -15 -10 -5 1	104
cct ttc tcc tct ccg ggc act gac ccc acc ttt ccg tgt att tac tgt Pro Phe Ser Ser Pro Gly Thr Asp Pro Thr Phe Pro Cys Ile Tyr Cys 5 10 15	152
agg cta tta aat atg atc atg acc cgc ctt gca ttt tca ttc atc acc Arg Leu Leu Asn Met Ile Met Thr Arg Leu Ala Phe Ser Phe Ile Thr 20 25 30	200
tgt tta tgc cca aat tta aag gaa gtt tgt ctc att ttg cca gaa aaa Cys Leu Cys Pro Asn Leu Lys Glu Val Cys Leu Ile Leu Pro Glu Lys 35 40 45	248
aat tgt aat agt cga cac gct gga ttt gta ggg cca sca aaa ttg cgg Asn Cys Asn Ser Arg His Ala Gly Phe Val Gly Pro Xaa Lys Leu Arg 50 65	296
cag tgaaactwkk ttcwcttcta aagcccttca tttcccacaa ggttaagctc Gln	349
togaaacccc atttgatoot tggttootat ttogatooto otttggaato tgaaaatogg	409
tctccatgtt gtatgcaaat taaaakttgc cttgtttgtt actcttccaa cacagggtat	469
cagggaraaa gaggcettat etgtteetee ateceeetg ttttgacaga etgetaagaa	529
ttcctcagga cttcctttgg ttggggattt tactttccca aaagtctgat ctgatttctt	589
tcaggggtag acaagcitgt cctagtgctc tgcttcaggt cttatcagaa gaaacccagg	649
aatagaaaag gtagatgcct tgacttttgt ccctgttgtg gggactaaag tgttttttgc	709
cagaattgtc aaaagctccg gttcaaactc tgtagagttt catggaaaaa caaaacaaaa	769 775

<210> 265 <211> 1075 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 198..431 <221> sig\_peptide <222> 198..260 <223> Von Heijne matrix score 6.90000009536743 seq LLACGSLLPGLWQ/HL <221> polyA\_site <222> 1064..1074 <400> 265 atatatttct gaggcagtac ccatctcact tgtaaactta aaagacaccg cagagatttg 60 agggactcag aagtcaaata gagtaggtta aaaacctctt atttttcaaa ttaattgttt 120 taagaaacaa gcatacctgt gtaagtgaaa tatcttaatt tgtgttgaat caagttagga 180 gacagagatt ctcatga atg tgt cct gtg ttc tca aag cag ctg cta gcc 230 Met Cys Pro Val Phe Ser Lys Gln Leu Leu Ala -20 -15 tgt ggg tct ctc cta cct ggg tta tgg cag cac ctc aca gcc aat cac 278 Cys Gly Ser Leu Leu Pro Gly Leu Trp Gln His Leu Thr Ala Asn His

tgg cct cca ttc tcc sct ttc ctc tgt aca gtt tgc tct ggt tcc tca Trp Pro Pro Phe Ser Xaa Phe Leu Cys Thr Val Cys Ser Gly Ser Ser	326
gag cag att tcc gag tat act gct tca gcc acg ccc cca ctg tgc cgt Glu Gln Ile Ser Glu Tyr Thr Ala Ser Ala Thr Pro Pro Leu Cys Arg	374
25 30 35  tcc ctg aac caa gag cca ttc gty tca aga gcc att cgt cca aag tac  Ser Leu Asn Gln Glu Pro Phe Val Ser Arg Ala Ile Arg Pro Lys Tyr	422
40 45 50 tct atc acc tagccattgt akccatacca agccgggctt cctacttccc Ser Ile Thr	471
55	531
totgotocco tiggittoct cotgiraari aaatotoaci gaccotigai goasciocaa goatatataa tatatatata ataaaaccai abtotaaaaa attoaaacca ggawaaataa	591
asccaraaat ttgtatggga aaaatctgca caaatttatt tggccagcat ggttatcatg	651
gctctattga atttatcctt gaccgtcttt aaagccaaag caaacgggat aaagtgatca	711 771
actacttacc tctcaatacc aaaaargaag caggaggcaa aatctctcaw taatttcata aaaacaattc ttakctgggc gcggtggctc wcacctgtar tcccaacact ttgggaggcc	831
saggtgggcg gatcatgagg tcgggagatc aamaccatcc tggctaacat ggtgaaaccc	891
catctctact aaaattacaa aaaattrgct gggcgaggtg gcgggcacct gtggtcccag	951
ctactcggga ggctgaggca agagaatggt gtgaacctca gggggcggag cctgcagtga	1011
gctgagateg caccactgca ctecageetg ggegacagtg agaeteegte teaaaaaaaa aaah	1071
<210> 266 <211> 981	
<212> DNA	·
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 279473	
<221> sig_peptide	
<222> 279362	
<223> Von Heijne matrix	
score 4.40000009536743 seg SCFLVALIIWCYL/RE	
beg beravalinera, all	
<221> polyA_signal <222> 944949	
<221> polyA_site <222> 970981	
<400> 266	
agaatcgtgt cttgtgtgcc ccggcggccg ggtgagctcc tcaaggtctc ggagggccga	60
gggcagacac cggcgggcgg gcggasgctt actgctctct ctcttccagg gccgtccggg	120 180
cgctgaggct cataggctgg gcttcccgaa gccttcatcc gttgcccggt tcccgggatc gggcccaccc tgccgccgag gaagaggacg accctgaccg ccccattgag ttttcctcca	240
gcaaagccaa ccctcaccgc tggtcggtgg gccatacc atg gga aag gga cat cag	296
Met Gly Lys Gly His Gln -25	
cgg ccc tgg tgg aag gtg ctg ccc ctc agc tgc ttc ctc gtg gcg ctg	344
Arg Pro Trp Trp Lys Val Leu Pro Leu Ser Cys Phe Leu Val Ala Leu -20 -15 -10	
atc atc tgg tgc tac ctg agg gag gag agc gag gcg gac cag tgg ttg	392
Ile Ile Trp Cys Tyr Leu Arg Glu Glu Ser Glu Ala Asp Gln Trp Leu	
-5 1 5 10	440
aga cag gtg tgg gga gag gtg cca gag ccc agt gat cgt tct gag gag	440

WO 99/31236 -188- PCT/IB98/02122

Arg Gln Val Trp Gly Glu Val Pro Glu Pro Ser Asp Arg Ser Glu Glu 15 20 25	
cct gag act cca gct gcc tac aga gcg aga act tgacggggtg cccgctgggg Pro Glu Thr Pro Ala Ala Tyr Arg Ala Arg Thr 30 35	493
ctggcaggaa gggagccgac asccgcctt cggatttgat ktcacgtttg cccgtgactg tcctggctat gcktgcgtcc tcagcactra argacttggc tggtggatgg ggcacttggc tatgctgatt cgcgtgaagg cggavcaaaa tctcagcaaa tcggaaactg ctcctscct ggctcttgat ktccaaggat tccatcggca aaacttctca ratccttggg gaaggtttca gttgcactgt atgctgttgg atttgccaag tctttgtata acataatcat gtttccaaag cacttctggt gacacttgtc atccagtgtt agtttgcagg taatttgctt tctgagatag aatatctggc agaagtgtga aactgtattg catgctgcgg cctgtgcaag gaacacttcc acatgtgagt tttacacaac aacaaatgaa aataaatttt aattttataa tatgggaaaa aaaaaaaa	553 613 673 733 793 853 913 973 981
<210> 267	
<211> 1031	• .
<212> DNA <213> Homo sapiens	
<220>	
<221> CDS	
<222> 12644	
<221> sig_peptide <222> 1292	
<223> Von Heijne matrix	•
score 4 seq LTFFSGVYGTCIG/AT	
•	
<221> polyA_signal <222> 10021007	
<222> 10021007  <221> polyA_site <222> 10201031  <400> 267	,
<222> 10021007  <221> polyA_site <222> 10201031  <400> 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg Met Leu Leu Ser Ile Thr Thr Ala Tyr Thr Gly Leu	50
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	50 98
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	98
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	98
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	98
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	98
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	98 146 194
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	98 146 194
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	98 146 194 242
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	98 146 194 242
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	98 146 194 242 290
<pre>&lt;222&gt; 10021007  &lt;221&gt; polyA_site &lt;222&gt; 10201031  &lt;400&gt; 267 acaccaagga g atg ctc ctt ctt agt att aca act gct tat aca ggt ctg</pre>	98 146 194 242 290

85 90 · 95	
85 90 95 gga aac agc tgc ttt aat acc cas ctg ctt akt atc tkg ggc ttt ctg	434
Gly Asn Ser Cys Phe Asn Thr Xaa Leu Leu Xaa Ile Xaa Gly Phe Leu	•
100 105 110	
tat tot gaa rac ago goo coa koa ttt goo ato tto aat ttt gtt cag	482
Tyr Ser Glu Xaa Ser Ala Pro Xaa Phe Ala Ile Phe Asn Phe Val Gln	
115 120 125 130	530
tct att tgc gca gcc gtg gca ttt ttc tac agc aac tac ctt ctc ctt Ser Ile Cys Ala Ala Val Ala Phe Phe Tyr Ser Asn Tyr Leu Leu	
135 140 145	
cac tgg caa ctc ctg gtc atg gtk atw ttt ggg ttt ttk gga aca att	578
His Trp Gln Leu Leu Val Met Val Ile Phe Gly Phe Xaa Gly Thr Ile 150 155 160	
tot the the act grg gaa tgg gaa set gee gee the gra see ege gge	626
Ser Phe Phe Thr Val Glu Trp Glu Xaa Ala Ala Phe Val Xaa Arg Gly	
165 170 175 . tot gao tao oga agt ato tgatotggtg toogtgaggg gacacgtatg	674
Ser Asp Tyr Arg Ser Ile 180	
acctcagaaa cacagctgga cacagagctt ggtggaagaa gtcgcctttg atcttcacta	734
tatattgggt gatgttcagt atggaaaatc aagggattaa gactgttaaa tcagccagag	794
tkggtgttca agtttacaga tatgagttat ttaaagcaag tagaataagg gaaagctgtt	854
ctgtcaactg taattgttca aagatgttgt ttttcatttc atctatctca attcttataa	914
tcatgttata gaatgtaaat gttttcttct ctctcctgct cttgttggaa gatcctgcct	974 1031
tgatttagaa tactaggcca tatgtcatat aaatattttt tctggaaaaa aaaaaaa	1031
<210> 268	
<211> 1283	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 91459	
<221> sig_peptide	
<222> 91330	
<223> Von Heijne matrix	
score 7.69999980926514	
seq LVLFLSLALLVTP/TS	
<221> polyA_site	
<222> 12711281	
400. 000	
<400> 268 tattccttgg agttccacga ctgaattaag actgttgtgg grdccataat tttcaaatac	60
ttgccctata ttcgtgttga gggttcacac atg agc aca tgg tat ttg gca ctt	114
Met Ser Thr Trp Tyr Leu Ala Leu -80 -75	
aat aag too tat aag aat aaa gac agc gtt agg att tat otc agc ttg	162
Asn Lys Ser Tyr Lys Asn Lys Asp Ser Val Arg Ile Tyr Leu Ser Leu	
-70 -65 -60	210
tgc aca gtg agc att aaa ttt aca tac ttt cat gat ata cag act aat Cys Thr Val Ser Ile Lys Phe Thr Tyr Phe His Asp Ile Gln Thr Asn	210
-55 -50 -45	
tgt ctt aca aca tgg aaa cat tcg aga tgc aga ttt tat tgg gca ttt	258
Cys Leu Thr Thr Trp Lys His Ser Arg Cys Arg Phe Tyr Trp Ala Phe	
-40 -35 -30 -25	
ggt ggt tcc att tta cag cac tca gtg gat ccc ctt gtt ttg ttc cta	306
Gly Gly Ser Ile Leu Gln His Ser Val Asp Pro Leu Val Leu Phe Leu	

	-
• •	
-10 -10	
age etg gee etg tta gtg aca eee act tee ace eet tet get aar ata	354.
Ser Leu Ala Leu Leu Val Thr Pro Thr Ser Thr Pro Ser Ala Lys Ile	
-5 1 5	
car age ett caa att gae ete eet gga gge tgg agg etg gee aet gae	402
Gln Ser Leu Gln Ile Asp Leu Pro Gly Gly Trp Arg Leu Ala Thr Asp	
10 15 20	
agg atc ttt acc ctc tcc ccc gta ccc atg gac rgc ccc ctc atc ctt	450
Arg Ile Phe Thr Leu Ser Pro Val Pro Met Asp Xaa Pro Leu Ile Leu	
25 30 35 40	
cat cag ttg taaaggtaga tatttgttcc ttggagtcca acatcatgct	499
His Gln Leu	
gttcagaata taatgagatc aatagttgaa aaactagata tacatgccac ccwgacaaag	559
ctattaagtt attaagtgtc agccctggat cttggcttat tgtgaaatgt taattatttt	619
atcactcyat taagaagetg tgggeteeat etcageattg aaaagggact aatttgetet	679
gttttggaat tgaattaget ttcaggecas cagggeactg tttggtaaat tgetttttee	739
agtactagca tgttttctcc ctccatagcc tctgttagct tctgagcttg taacctccag	799
ggaaavatga gaatattcac ccttttaata tgtgtagaga ccatgcaaga ccattgtctt	859
ctaataatta gaaatactta gccagattct ctatagtaaa cccggagatt gggagggctg	919
ctttctactt ggtgcatcct tctgcgcttc taatgatttt taaaaatctg ttaataattg	979
atgttttctg gctgggcaca gtggctcacg cctgtaatcc cagcactttg ggaggccaag	1039
gagggcagat catgaggtca ggagattgar accatcctgg ctaacacggt gaaaccccgt	1099
ctctactaaa aatacaaaar aattakeegg geatggtagt gggegeetgt gtacceaget	1159
actggggagg ctgaggcarg araatcgctt gaacctggga ggcggaggtt gcastragct	1219
gagatggtgc caccgcactc tagcctgggt gacagagcga gacttcattt caaaaaaaaa	1279
aamc	1283
eg it	
<210> 269	
<211> 1777	
<212> DNA	

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 70..327

<221> sig\_peptide

<222> 70..147

<223> Von Heijne matrix score 9.60000038146973 seq WLIALASWSWALC/RI

<221> polyA\_signal <222> 1741..1746

<221> polyA\_site <222> 1763..1774

<400> 269

ageceggttt egtgeeegeg geegaetgeg easetgteeg egagtetgag ataettacag 60 111 agagetaca atg gaa aag tee tgg atg etg tgg aac ttt gtt gaa aga tgg Met Glu Lys Ser Trp Met Leu Trp Asn Phe Val Glu Arg Trp -25 -20 cta ata gcc ttg gct tca tgg tct tgg gct ctc tgc cgt att tct ctt 159 Leu Ile Ala Leu Ala Ser Trp Ser Trp Ala Leu Cys Arg Ile Ser Leu -5 tta cct tta ata gtg act ttt cat ctg tat gga ggc att atc tta ctt 207 Leu Pro Leu Ile Val Thr Phe His Leu Tyr Gly Gly Ile Ile Leu Leu 10 15 255 ttg tta ata ttc ata tca atw kca ggt att ctg tat aaa ttc cas gat

```
Leu Leu Ile Phe Ile Ser Ile Xaa Gly Ile Leu Tyr Lys Phe Xaa Asp
                                     30
                 25
                                                                      303
gta ttg ctt tat ttt ccw kaa cag yya tcc tct tca cgt ctt tat gat
Val Leu Leu Tyr Phe Pro Xaa Gln Xaa Ser Ser Ser Arg Leu Tyr Asp
                                 45
tcc cat gcc cac tgg cmt tcg rca taaaaaaatt ttcatcagaa ccaaagatgg
                                                                      357
 Ser His Ala His Trp Xaa Ser Xaa
         55
 aatacgtctg aatcttattt tgatacgata cactggagac aattcaccct attccccaac
                                                                      417
 tataatttat tttcatggga atgcaggcaa cataggtcac aggttggcca aatgcattac
                                                                       477
 ttatgttggt taacctcaaa gttaaccttt tgctggttga ttatcgagga tatggaaaaa
                                                                       537
                                                                      597
 gtgaaggaga agcaagtgaa gaaggactct acttagattc tgaagctgtg ttagactacg
                                                                       657
 tgatgactag acctgacctt gataaaacaa aaatttttct ttttggccgt tccttgggtg
                                                                       717
garcagtggc tattcatttg gcttctgaaa attcacatag gatttcagcc attatggtgg
agaacacatt tttaagcata ccacatatgg ccagcacttt attttcattc tttccgatgc
                                                                       777
                                                                       837 .
 gttaccttcc tttatggtgc tacaaaaata aatttttgtc ctacagaaaa atctctcagt
 gtagaatgcc ttcacttttc atctctggac tctcagatca attaattcca ccagtaatga
                                                                       897
 tgaaacaact ttatgaactc tccccatctc ggactaagan attagccatt tttccagatg
                                                                       957
 ggactcacaa tgacacatgg cagtgccaag gctatttcac tgcacttgaa cagttcatca
                                                                     1017
                                                                      1077
 aaqaaqtcqt aaagagccat tctcctgaag aaatggcaaa aacttcatct aatgtaacaa
 ttatataatg tttccctttt tgattattgc attgtatttt aatttgtgca gaatgataaa
                                                                      1137
 gaatgttcct tttagaagtg tgttatgtct gtacctgtct gaagagtgac attaaacttt
                                                                      1197
                                                                      1257
 qaaaggactt cactgctcct ttacgatatt ccaaatagtt ttttacattg gaaaaactaa
 ttcttgggat tctttcatac attttcatca aaactttcag tgtgattatg tattcatatc
                                                                      1317
 ttcagtttaa tatgtcagta taatagatat tgttcaaaag tttcttgttg ctaaagtggt
                                                                      1377
                                                                      1437
 qtaatctgtt acacagatga atagctagat gtggaaagag atatgtaaac aagaaacctt
 tgggtattgt ttcttaagta aatattggga caatcatggt aagcaaactt agttctgtaa
                                                                      1497
 ctgcattttt caccttaaaa gttaaatgaa atgcatgatg gtattttatt ccttgaatta
                                                                      1557
 tgcaatgcaa cattttacat gtaaatagca ctggtcatat actgatgtat atggttatct
                                                                      1617
                                                                      1677
 gggttatatc tattttatg taaactctat ttttgttttt ggcaagaagt gaaattgaga
 cttatgtgca ggttgccatt gaattttgct ctggtgaatg ctgagatcca gctttttctt
                                                                      1737
 acaaataaat gggaccctgt tttccaaaaa aaaaaaamcm
                                                                      1777
 <210> 270
 <211> 970
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> CDS
```

```
-15
                                 -10
aca gga ccc tgg ggg gct gtt gcc acc tcc gcc ggg ggc gag gag tcg
                                                                      146
Thr Gly Pro Trp Gly Ala Val Ala Thr Ser Ala Gly Gly Glu Glu Ser
                                                                      194
ctt aag tgc gag gac ctc aaa gtg gga caa tat att tgt aaa gat cca
Leu Lys Cys Glu Asp Leu Lys Val Gly Gln Tyr Ile Cys Lys Asp Pro
aaa ata aat gac gct acg caa gaa cca gtt aac tgt aca aac tac aca
                                                                      242
Lys Ile Asn Asp Ala Thr Gln Glu Pro Val Asn Cys Thr Asn Tyr Thr
                                    40
            . 35
                                                                      290
get cat gtt tee tgt ttt eea gea eee aac ata act tgt aag gat tee
Ala His Val Ser Cys Phe Pro Ala Pro Asn Ile Thr Cys Lys Asp Ser
                                 55
                                                                      338
agt ggc aat gaa aca cat ttt act ggg aac gaa gtt ggt ttt ttc aag
Ser Gly Asn Glu Thr His Phe Thr Gly Asn Glu Val Gly Phe Phe Lys
                            70
                                                                      386
ccc ata tct tgc cga aat gta aat ggc tat tcc tac aat gag cag tcg
Pro Ile Ser Cys Arg Asn Val Asn Gly Tyr Ser Tyr Asn Glu Gln Ser
                                                                      434
cat gtc tct ttt tct tgg atg gtt ggg agc aga tcg att tta cct tgg
His Val Ser Phe Ser Trp Met Val Gly Ser Arg Ser Ile Leu Pro Trp
95
                                                             110
                    100
                                         105
ata ccc tgc ttt ggg ttt gtt aaa btt tyg cac tgt agg gtt'tkg tgg
                                                                      482
Ile Pro Cys Phe Gly Phe Val Lys Xaa Xaa His Cys Arg Val Xaa Trp
                                     120
                115
                                                                      537
aat tgg gag cct aat tgatttcaty cttatttcaa tgcagattgt tggaccttca
Asn Trp Glu Pro Asn
            130
                                                                      597
aatggaagta gttacattat agattactat ggaaccagac ttacaagact gagtattact
aatgaaacat ttagaaaaac gcaattatat ccataaatat tttttaaaag aaacagattt
                                                                       657
gagcctcctt gattttaata gagaacttct agtgtatgga tttaaagatt tctctttttc
                                                                       717
attcatatac cattttatga gttctgtata attttttgtg gtttttgttt tgttgagtta
                                                                       777
aagtatatta tigigagati tatitaatag gacticctit gaaagcigta taatagigit
                                                                       837
tctcgggctt ctgtctctat gagagatagc ttattactct gatactcttt aatcttttac
                                                                       897
aaaggcaagt tgccacttgt catttttgtt tctgaaaaat aaaagtataa cttattcaca
                                                                       957
aaaaaaaaa mms
                                                                       970
```

<211> 645

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 90..383

<221> sig\_peptide

<222> 90..200

<223> Von Heijne matrix
 score 4.90000009536743
 seq MLIMLGIFFNVHS/AV

<221> polyA\_signal

<222> 609..614

<221> polyA\_site

<222> 632..643

<400> 271

atttctgccc ccctgcgagg gcatcctggg ctttctccca ccgctttccg agcccgcttg

cacc																	
	tcgg	icg a	tçcc	cgac	t co	cttc	ttt	atg Met	gcg Ala	tcg Ser -35	ctc Leu	ctg Leu	tgc Cys	Cys	999 Gly -30	113	
									:-			+~~		ata	atc	161	
ccg	aag	ctg	gcc	gcc	tgc	ggc	atc	gtc	CEC	age	gee	-99	990	919	73.	101	
Pro	Lys	Leu	Ala	Ala	Cys	Gly	Ile	Val	Leu	Ser	Ala	Trp	GlÀ	Val	TTE		
				-25	-	_			-20					-15			
										a+ a	c=+	+ c c	act	ata	tta	209	
atg	ttg	ata	atg	CEC	gga	ata	EEE	ttc	aat	gcc	Cat	-	gee	9.59	T	203	
Met	Leu	Ile	Met	Leu	Gly	Ile	Phe	Phe	Asn	Val	His	Ser	Ala	vaı	Leu		
			-10					-5					1				
			gtt		++0	200	~~~	222	cat	+++	nan	aac	aac	ccc	car	257	
att	gag	gac	get	-	-1	acg	909	-	900	7	203	2	220	D=0	Cln		
Ile	Glu	Asp	Val	Pro	Phe	Thr	Glu	Lys	Asp	Pne	GIU	Asn	GIY	PIO	GIII		
	5			,		10					15						
		+	aac	ctt	tac	ran	C22	ktc	·acc	tac	aac	tat	ttc	atc	act	305	
aac	ala -	Lac	200			Y	03-	Y	050	m	200	Cvc	Dhe	Tle	בו ב		
Asn	Ile	Tyr	Asn	ьeu		хаа	GIN	Aaa	261		MSII	Cys	FIIC	110	7.5		
20					25					30					35		
~~=	aac	ctt	tac	ctc	ctc	ctc	gga	aac	ttc	tct	ttc	tqc	caa	ktt	cgg	3,53	
gca	990	7	m	7	7	7 000	23	61	Dho	Cox	Dhe	Cve	Gln	Yaa	Arg		
Ala	GIÀ	Leu	Tyr	Leu	Leu	Leu	GIÀ	GIY		261	PILE	Cys	0111	7.00	9		
				40					45					50			
ctc	aat	aag	cgc	aag	gaa	tac	atq	ata	cac	tag	aacc	ccq	qcgc	gttt	CC	403	
-	2	7	7~~	1	2111	There	Met	17-1	Ara		<i>-</i>	-		_			
Leu	Asn	гÀг	Arg	Lys	GIU	ıyı	Met		HIG								
			55 ·					60		•							
cca	et de	acc	ccct	cctci	ta t	ttaaa	aract	t cc	ctac	accg	tkt	cacc	cag	gtcg	cgtccc	. 463	
CC9.			~~~			~~~	-+	~ ++	+ ~ ~ ~	~~~~	rar	arac	tga	atcc	cttctc	523	
acc	cttg	ccg	gege		ra r	ggga	99	9		3336	101				****	583	
cca	tctc	tgg	catc	cggc	CC C	cgtg	gara:	r gg	ctga	ggct	999	gggc	tgt	tccg	tctctc		
cac	cctt	cac	tata	tccc	at a	tctc	aata	a ag	agaa	tctg	ctc	tctt	caa	aaaa	aaaaaa	643	
		- 5			-				•	_						645	
my																	
										•							
																•	
				1													
<21	0 > 2	12															
	0> 2 1> 7																
<21	1> 7	73															
<21 <21	1> 7 2> D	73 NA	coni	one													
<21 <21	1> 7 2> D	73 NA	sapi	ens													
<21 <21	1> 7 2> D	73 NA	sapi	ens													
<21 <21 <21	1> 7 2> D 3> H	73 NA	sapi	ens													
<21 <21 <21 <22	1> 7 2> D 3> H 0>	73 NA omo	sapi	ens						-							
<21 <21 <21 <22 <22	1> 7 2> D 3> H 0> 1> C	73 NA omo		ens													
<21 <21 <21 <22 <22	1> 7 2> D 3> H 0> 1> C	73 NA omo		ens													
<21 <21 <21 <22 <22	1> 7 2> D 3> H 0> 1> C	73 NA omo		ens													
<21 <21 <21 <22 <22 <22 <22	1> 7 2> D 3> H 0> 1> C 2> 3	73 NA omo DS 32	541														
<21 <21 <21 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> 1> C 2> 3	73 NA omo DS 32	541 epti														
<21 <21 <21 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> 1> C 2> 3	73 NA omo DS 32	541 epti														
<21 <21 <21 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> 1> C 2> 3 1> s 2> 3	73 NA omo DS 32	541 epti	de	trix	:											
<21 <21 <21 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> 1> C 2> 3 1> s 2> 3 3> V	73 NA omo DS 32	541 epti 376 eijn	de e ma			7										
<21 <21 <21 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V	73 NA omo DS 32 ig_p 32	541 epti 376 eijn 3.5	de e ma 9999	9904	6325	7										
<21 <21 <21 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V	73 NA omo DS 32 ig_p 32	541 epti 376 eijn	de e ma 9999	9904	6325	7										
<21 <21 <21 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V	73 NA omo DS 32 ig_p 32	541 epti 376 eijn 3.5	de e ma 9999	9904	6325	7										
<21 <21 <22 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V s s	73 NA omo DS 32 ig_p 32 on H core	541 epti 376 eijn 3.5 LPCC	de e ma 9999 LLWS	9904	6325	7										
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V s 1> F	73 NA omo DS 32 ig_p 32 core eq F	541 epti 376 eijn 3.5 LPCC	de e ma 9999 LLWS	9904	6325	7										
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V s 1> F	73 NA omo DS 32 ig_p 32 on H core	541 epti 376 eijn 3.5 LPCC	de e ma 9999 LLWS	9904	6325	7										
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V s 1> F	73 NA omo DS 32 ig_p 32 core eq F	541 epti 376 eijn 3.5 LPCC	de e ma 9999 LLWS	9904	6325	7										
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V 5 2> 7	DS 32 ig_p 32 on H core eq F	epti 376 eijn 3.5 LPCC	de e ma 9999 LLWS nal	9904	6325	7										
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V 52> 7	DS 32 ig_p 32 on H core eq F	epti 376 eijn 3.5 LPCC	de e ma 9999 LLWS nal	9904	6325	7										
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V 52> 7	DS 32 ig_p 32 on H core eq F	epti 376 eijn 3.5 LPCC	de e ma 9999 LLWS nal	9904	6325	7										
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 2> 3 1> S 2> 3 3> V 52> 7	DS 32 ig_p 32 on H core eq F	epti 376 eijn 3.5 LPCC	de e ma 9999 LLWS nal	9904	6325	7										
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 1> 3 1> S 2> 3 3> V 52> 7	DS 32 ig_p 32 on H score eq F	541 epti 376 eijn 3.5 LPCC _sig 744 _sit 773	de e ma 9999 LLWS nal	9904 VFNF	6325 /ES											
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 2> D 3> H 0> C 1> 3 1> S 2> 3 3> V 52> 7	DS 32 ig_p 32 on H score eq F	541 epti 376 eijn 3.5 LPCC _sig 744 _sit 773	de e ma 9999 LLWS nal	9904 VFNF	6325 /ES		ia ti	catt:	a a a o o	t ct:	aaac	aaaa	tta	caattto		0
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 D	DS 32 ig_p 32 on H score eq F	epti 376 eijn 3.5 LPCC _sig 744 _sit 773	de e ma 9999 LLWS nal e	9904 VFNF	6325 P/ES	:tatt	ia ti	catt:	aaagi	t cta	aaac	aaaa	ttg	caattto	: 6 1 12	
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 D	DS 32 ig_p 32 on H core seq F ooly 761	epti 376 eijn 3.5 LPCC 744 sit 773	de e ma 9999 LLWS nal e	9904 VFNF	6325 P/ES	tatt:	aa ga	atta	ccct	c aa	atgc	taga	agc	tgtctag	12	0
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 D	DS 32 ig_p 32 core eq F colyA 761	epti 376 eijn 3.5 LPCC 744 sit 773 atgc	de e ma 9999 LLWS nal e	9904 VFNF	6325 P/ES	tatt atga	aa ga ga ti	atta taga	ccct tgtg	c aaa	atgc ataa	taga ccaa	agc gtt	tgtctag tattcag	; 12 ; 18	0
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 D	DS 32 ig_p 32 core eq F colyA 761	epti 376 eijn 3.5 LPCC 744 sit 773 atgc	de e ma 9999 LLWS nal e	9904 VFNF	6325 P/ES	tatt atga	aa ga ga ti	atta taga	ccct tgtg	c aaa	atgc ataa	taga ccaa	agc gtt	tgtctag tattcag	; 12 ; 18	0
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 D 2> B 0> C 1> 3 S 1> S 1> S 1> F 1> 7 D 1> C	DS 32 ig_p 32 core eq F colyA 761	epti 376 eijn 3.5 LPCC 744 sit 773 atgc	de e ma 9999 LLWS nal e	9904 VFNF ca t ac a	eagtt	tatt aatga ctcag	aa ga ga ti it ta	atta taga atta	ccct tgtg ctct	c aaa c caa c ac	atgc ataa ccat	taga ccaa aaac	agc gtt agt	tgtctag tattcag aatgact	12 18 12 24	0 0 0
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 D	DS 32 ig_p 32 core eq F 239 272 attc accgg actt	epti 376 eijn 3.5 LPCC 744 sit 773 atgc ttgt gtac	de e ma 9999 LLWS nal e cttt	9904 VFNF ca t ac a sat t	cagtt tagtt tagtt catct gtagt	tatt aatga tcag tggtt	aa ga ga ti it ta ic ca	attad tagad attad aatc	ccct tgtg ctct ttgc	c aac c ac t tt	atgc ataa ccat gtgt	taga ccaa aaac atct	agc gtt agt cat	tgtctag tattcag aatgact ttaattt	12 18 24 23 30	0
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 D	DS 32 ig_p 32 core eq F 239 272 attc accgg actt	epti 376 eijn 3.5 LPCC 744 sit 773 atgc ttgt gtac	de e ma 9999 LLWS nal e cttt	9904 VFNF ca t ac a sat t	cagtt tagtt tagtt catct gtagt	tatt aatga tcag tggtt	aa ga ga ti it ta ic ca	attada taga attad aatc aatc	ccct tgtg ctct ttgc cga	c aac c ac t tt	atgc ataa ccat gtgt ctt	taga ccaa aaac atct cct	agc gtt agt cat tgt	tgtctag tattcag aatgact ttaattt tgt	12 18 12 24	0
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 D	DS 32 ig_p 32 core eq F 239 272 attc accgg actt	epti 376 eijn 3.5 LPCC 744 sit 773 atgc ttgt gtac	de e ma 9999 LLWS nal e cttt	9904 VFNF ca t ac a sat t	cagtt tagtt tagtt catct gtagt	tatt aatga tcag tggtt	aa ga ga ti it ta ic ca	attada taga attad aatc aatc	ccct tgtg ctct ttgc cga	c aac c ac t tt	atgc ataa ccat gtgt ctt	taga ccaa aaac atct cct	agc gtt agt cat tgt	tgtctag tattcag aatgact ttaattt tgt	12 18 24 23 30	0
<21 <21 <22 <22 <22 <22 <22 <22 <22 <22	1> 7 D	DS 32 ig_p 32 core eq F 239 272 attc accgg actt	epti 376 eijn 3.5 LPCC 744 sit 773 atgc ttgt gtac	de e ma 9999 LLWS nal e cttt	9904 VFNF ca t ac a sat t	cagtt tagtt tagtt catct gtagt	tatt aatga tcag tggtt	aa ga ga ti it ta ic ca	attada taga attad aatc aatc	eccto tgtgo etcto ttgo ega Arg	c aac c ac t tt	atgc ataa ccat gtgt ctt	taga ccaa aaac atct cct	agc gtt agt cat tgt	tgtctag tattcag aatgact ttaattt tgt Cys	12 18 24 23 30	0

ttg ctt tgg tct gtg ttc aat cca gag agc tta aat tgt cat tat ttt Leu Leu Trp Ser Val Phe Asn Pro Glu Ser Leu Asn Cys His Tyr Phe
-5 1 5

ctt cag gag aaa ctg ctg ggc ttc ctg tgg ctt tgt ttt ctt agt tac Leu Gln Glu Lys Leu Leu Gly Phe Leu Trp Leu Cys Phe Leu Ser Tyr 25 30 35 40  ttt ttc cgt gcc gtg tat ttt tta att gat ttt tct tct ttt act Phe Phe Arg Ala Val Tyr Phe Leu Ile Asp Phe Ser Ser Phe Thr 45 50 55  tgaaaagaaa gtgttttatt ttcaaatctg gtccatattt acattctagt tcagagccaa gcttcaaact gtacagaatt tccactgtaa ttaaaactat ttagtgttag ttataaatag 661 ccttcaaaaa gagagattct ccattacacg atcacctgca tcacagccca tggtgaatgt 721 atgttctgc atagcgaaat aaaaatggca aatgcactga aaaaaaaaaa
Phe Phe Arg Ala Val Tyr Phe Leu Ile Asp Phe Ser Ser Phe Thr 45 50 55  tgaaaagaaa gtgttttatt ttcaaatctg gtccatattt acattctagt tcagagccaa 601 gccttaaact gtacagaatt tccactgtaa ttaaaactat ttagtgttag ttataaatag 661 ccttcaaaaa gagagattct ccattacacg atcacctgca tcacagccca tggtgaatgt 721 atgttctgc atagcgaaat aaaaatggca aatgcactga aaaaaaaaaa
gecttaaact gtacagaatt tecactgtaa ttaaaactat ttagtgttag ttataaatag cetteaaaaa gagagattet ecattacacg atcacetgea teacagecea tggtgaatgt 721 atgtttetge atagegaaat aaaaatggea aatgeactga aaaaaaaaaa aa 773   <210> 273 <211> 566 <212> DNA <213> Home sapiens  <220> <221> CDS <222> 43222  <221> Sig_peptide <222> 43177 <223> Von Heijne matrix score 4 seq ENFLSLLSKSCSA/DP
ccttcaaaaa gagagattct ccattacacg atcacctgca tcacagccca tggtgaatgt 721 atgtttctgc atagcgaaat aaaaatggca aatgcactga aaaaaaaaaa
<pre>&lt;210&gt; 273 &lt;211&gt; 566 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 43222  &lt;221&gt; sig_peptide &lt;222&gt; 43177 &lt;223&gt; Von Heijne matrix</pre>
<pre>&lt;211&gt; 566 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 43222  &lt;221&gt; sig_peptide &lt;222&gt; 43177 &lt;223&gt; Von Heijne matrix</pre>
<pre>&lt;211&gt; 566 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 43222  &lt;221&gt; sig_peptide &lt;222&gt; 43177 &lt;223&gt; Von Heijne matrix</pre>
<pre>&lt;211&gt; 566 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 43222  &lt;221&gt; sig_peptide &lt;222&gt; 43177 &lt;223&gt; Von Heijne matrix</pre>
<pre>&lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 43222  &lt;221&gt; sig_peptide &lt;222&gt; 43177 &lt;223&gt; Von Heijne matrix</pre>
<pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 43222  &lt;221&gt; sig_peptide &lt;222&gt; 43177 &lt;223&gt; Von Heijne matrix</pre>
<pre>&lt;221&gt; CDS &lt;222&gt; 43222  &lt;221&gt; sig_peptide &lt;222&gt; 43177 &lt;223&gt; Von Heijne matrix</pre>
<222> 43222  <221> sig_peptide  <222> 43177  <223> Von Heijne matrix
<221> sig_peptide <222> 43177 <223> Von Heijne matrix score 4 seq ENFLSLLSKSCSA/DP
<222> 43177 <223> Von Heijne matrix score 4 seq ENFLSLLSKSCSA/DP
<223> Von Heijne matrix score 4 seq ENFLSLLSKSCSA/DP
score 4 seq ENFLSLLSKSCSA/DP
seq ENFLSLLSKSCSA/DP
<221> polyA_signal
<2215 polya_signal
<222> 530535
<221> polyA_site <222> 555566
2222 333300
<400> 273
aacgagtgga ggtgtggcta gtggctgtga tgagataaat cc atg cat agc ctt 54 Met His Ser Leu -45
ttc att gcg agc ttg aaa gtt ctt ttc tat tac agt ttt agc ttt agg 102
Phe Ile Ala Ser Leu Lys Val Leu Phe Tyr Tyr Ser Phe Ser Phe Arg -40 -35 -30
ttt aat tgg ttc gac tgc ctt ctc cac aat ttg ggc gag aat ttc ctt 150
Phe Asn Trp Phe Asp Cys Leu Leu His Asn Leu Gly Glu Asn Phe Leu
-25 -20 -15 -10 agc ctt ctc agc aaa agt tgt tct gcg gac ccg tct ggg tca act ttc 198
Ser Leu Leu Ser Lys Ser Cys Ser Ala Asp Pro Ser Gly Ser Thr Phe
-5 1 5
atg agg gac att gag aca aac aaa tgaaatatgg gttaaagtac tctgagcagc 252 Met Arg Asp Ile Glu Thr Asn Lys 10 15
tacaaaaaga araccagtct atcctgctgg agacagtggc cacgtgaara aagagctctt 312
gragtatgaa agaccacatg gaaagagag ccacatggaa ccaacagtca gratcttggt 372
ttcggacacg tgaaraaatt catctcarac tgtgtatcct aaatcaggca cttgctgaat 432 ctaactacat gagtgagacc agttgacaac acatggagca racatgagct gttctcagtg 492
artectacae aaatteetga etcacaacae tgtgagcaat aaaatggttg ttattttaag 552
ccaaaaaaaa aaaa 566

-10

cetectgece egececatta aaacagttet tttgttaaaa aataveetaa tggtecaact

ttgctgtctg ttcttccaaa tgtttataat acacattatt tataaatatg tctgtttggg

aagctaagaa caagctagtt tttacaacac aaatggaaat aaatgcaatt attataaaaa

10

60 117

165

213

261

321

381

441

WO 99/31236

```
<210> 274
<211> 455
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 115..231
<221> sig peptide
<222> 115..180
<223> Von Heijne matrix
     score 5
     seq HLFVTWSSQRALS/HP
<221> polyA_signal
<222> 419..424
<221> polyA_site
<222> 445..455
<400> 274
aacctgccag tkatgcaaat gccaaaatgt gggtcatcat atagtatatt tgaaaccttt
ctgaacatgt acaccacca atgctagagg ctgacttgga aaccggtggg tgca atg
ccc gag gct gtg gaa caa tca gcc cat ctc ttt gtg acc tgg agc agt
Pro Glu Ala Val Glu Gln Ser Ala His Leu Phe Val Thr Trp Ser Ser
                        -15
cag agg gcc ctc agt cac ccc gcc cca ttc ctc acc ara raa aar aat
Gln Arg Ala Leu Ser His Pro Ala Pro Phe Leu Thr Xaa Xaa Lys Asn
                    1
                                   5
-5
cca ttt cta tgg aag ctc tgacgtaact tcagtgtttt ctacaatact
Pro Phe Leu Trp Lys Leu
```

<210> 275 <211> 673 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 232..384 <221> sig\_peptide <222> 232..300 <223> Von Heijne matrix score 3.70000004768372 seq FFLCAAFPLGAGV/KM <221> polyA\_signal <222> 650..655 <221> polyA\_site

15

tycaaaaaa aaaa

<222> 662..673

<400> 275 <sup>1</sup> / <sub>40</sub>	
atttggcttg cagactgcct tctatcccag aacagctgag aaatctatga agctgagatt	60
ctgaaggacc cagcttaggt tcttccactt aggcctcaat tcccttcctt ttccaggggc	120
agcettagtt teccatggee etgaaacaca cacatttece cetteettte ecagaageea	180
ctggccccc atagcaccca gtgcatcctt tttacaagtg gaagaactag g atg gct Met Ala	237
ttc caa agt ctt cta gaa atg aag ttc ttt ctc tgt gca gct ttc ccc	285
Phe Gln Ser Leu Leu Glu Met Lys Phe Phe Leu Cys Ala Ala Phe Pro -20 -15 -10	
ctt gga gca gga gtg aag atg ttt cat tat ctt ggg cct ggg aaa cca	333
Leu Gly Ala Gly Val Lys Met Phe His Tyr Leu Gly Pro Gly Lys Pro	
-5 1 5 10	
ctt cyy cag gct tet eec tee eec cae eec cat agg ame agg att tgg	381
Leu Xaa Gln Ala Ser Pro Ser Pro His Pro His Arg Xaa Arg Ile Trp	
15 20 25	
cct tagettetgg geetatesge tgeetteeet ettytteeta ceacetette	434
Pro	404
tgccttcctt trawctctgt tgggcttggg gatcttagtt ttcttttgtt tatttcccat	494
ctcattttt tcttctggtc agtttttta agggggggtg ttgtggtttt ttgttttgt	554 614
tttgcttctg aaaaarcatt tgcctttctt cctotcccaa cataacaatc gtggtaacag	673
aatgcgactg ctgatttacc gatgtattta atgtaagtaa aaaaaggaaa aaaaraaaa	, 0,3
<210> 276	
<211> 639	
<212> DNA	
<213> Homo sapiens	
" "	
<220>	
<221> CDS	
<222> 143427	
<221> sig_peptide	
<222> 143286 .	
<223> Von Heijne matrix	
score 7.5	
seq FVILLFIFTVVS/LV	
<221> polyA_signal	
<222> 606611	
<pre>&lt;221&gt; polyA_site</pre>	
<222> 628639	
<400> 276	
aatcgcttca gcagcatect ctcagacaag agccactatt tctgattcag atcacctgtc	60
atcgaagttt aaagaagggg aaacaggaga cagaaataca ctgaaccaaa aagattcaaa	120
agagcaagtg gaatctctaa ga atg gct tcc agc cac tgg aat gaa acc act	172
Met Ala Ser Ser His Trp Asn Glu Thr Thr	
-45 -40	
acc tot gtt tat cag tac oft ggt ttt caa gtt caa aaa att tac oot	220
Thr Ser Val Tyr Gln Tyr Leu Gly Phe Gln Val Gln Lys Ile Tyr Pro	
-35 -30 -25	
ttc cat gac aac tgg aac act gcc tgc ttt gtc atc ctg ctt tta ttt	268
Phe His Asp Asn Trp Asn Thr Ala Cys Phe Val Ile Leu Leu Phe	
-20 -15 -10	
ata ttt aca gtg gta tct tta gtg gtg ctg gct ttc ctt tat gaa gtg	316
Ile Phe Thr Val Val Ser Leu Val Val Leu Ala Phe Leu Tyr Glu Val	
-5 1 5 10	
ctt gam wgc tgc tgc tgt gta aaa aac aaa acc gtg aaa gac ttg aaa	364
Leu Xaa Xaa Cys Cys Cys Val Lys Asn Lys Thr Val Lys Asp Leu Lys	

agt gaa ccc aac cct ctt ara akt atg atg gac aac atc aga aaa egt Ser Glu Pro Asn Pro Leu Xaa Xaa Met Met Asp Asn Ile Arg Lys Arg 30 gas act gaa gtg gtc taacactcta taraaaatga acaaaatct tgaaagcagc Glu Thr Glu Val Val 45 tcaacctctt ctgaraaaaa aaatatattc tgaggccaac tgttgctaca aaacaaatct tgactgaatg gttaaaacat ttctagtara aggggaaaaa aaakttaaac atgcactgtt tggtgtgtata secattcat taaatataca gtaaaactyc aaaaaaaaaaa aa	15 20 25	
Ser Glu Pro Aan Pro Leu Xaa Xaa Met Met Aap Aan 11e Arg Lys Arg 30 gaa act gaa gtg gtc taacactcta taraaaatga acaaaatct tgaaagcagc Glu Thr Glu Val Val 45 tcaacctctt ctgaraaaaa aaataattc tgaagccaac tgttgctaca aaacaaatct tgactgaatg gttaaaacaat ttctagtara aggggaaaaa aaakttaaac atgacctgtt tggtgtata sccattcat taaatataca gtaaaactyc aaaaaaaaaa aa <pre></pre>		412
30 35 40  Gaa act gaa gtg gtc taacactcta taraaaatga acaaaatct tgaaagcagc Glu Thr Glu Val Val  45  tcaacctctt ctgaraaaaa aaatatattc tgaggcaaac tgttgctaca aaacsaattc tgactgaatg gttaaaacat ttctagtara aggggaaaaa aaakttaaac atgcactgtt tgtgtgtata sccatttcat taaatataca gtaaaactyc aaaaaaaaaa aa  467  467  tcaacctctct ctgaraaaaa aaatattc tgaggcaaac tgttgctaca aaacsaattc tgactgaatg gttaaaacat ttctagtara aggggaaaaa aaakttaaac atgcactgtt tgtgtgtata sccatttcat taaatataca gtaaaactyc aaaaaaaaaa aa  468  4210 277  4211 772  4212 DNA  4213 Homo sapiens  4220 221 Se4 .463  4221 sig peptide 4222 284 .479  4223 Von Heijne matrix score 3.79999995231628 seq TFINITUMIGNIC/QR  4221 polyA site 4222 762 .772  4400 277  acagctgggg ctttgtcttc tttattgcta ggagaatgta gcaatagaag ttctcatcgc cctgtattgc acttttggtt ttaaggactg gacccagagt tcctgaaagc caaactcat aagctgctca gtaagttcca agcacatagc cggctkhggg atgcattcg gtcgaaggtc gtgtgaatgaa ggtagagcag gcaggagtt tgtcttacc agtacctga agaacggtgc cacttcctga gtgagctcac ttaccttccc tgaatggtga ggc atg gat gaa tat gtgtgaatgaa ggtagagcagagcagcagcagcagcagcagcagcagcagcagc	Ser Glu Pro Asn Pro Leu Xaa Xaa Met Met Asp Asn Ile Arg Lys Arg	
Gau act gas gt gt tt tastatic tassasays densett systym of the first Glu Val Val  45  Casacctctt ctgaraaaaa aaatatatt tgaggcaac tgttgctaca aaacaaatt tgactgatgt gttaaaacat ttctagtara aggggaaaaa aaakttaaac atgcactgtt tgtgtgtata sccattcat taaatataca gtaaaactyc aaaaaaaaaa aa 639  4210> 277  4211> 772  4211> 772  4212> DNA  4213> Homo sapiens  4220> 4221> sig_peptide  4222> 284379  4223> Von Heijne matrix score 3.7999995231628 seq TFINITUMLGSLC/OR  4221> polyA_site  4222> 762772  4400> 277  4000 277  4000 277  4000 277  4000 277  4001 277  4001 277  4002 277  4003 277  4003 277  4005 277  4005 277  4005 277  4005 277  4005 277  4005 277  4007 277  4008 277  4008 277  4008 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  4009 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 277  400 27	30 35 40	
tgactgaatg gttaaaaaa aaatatattc tgagggcaac tgttgctaca aaacaaattc tgactgaatg gttaaaaacat ttctagtara aggggaaaaa aaakttaaac atgcactgtt tgtgtgtata sccatttcat taaatataca gtaaaactyc aaaaaaaaaa aa 639  \[ \frac{210}{277} \] \{211}  772 \{211}  772 \{212}  DNA \{213}  Homo &apiens \] \[ \{220}{221}  CDS \{221}  Sig_ peptide \{222}  284  .463  \[ \{221}  sig_ peptide \{222}  284  .463  \[ \{221}  sig_ peptide \{222}  284  .463  \[ \{221}  polyA_ site \{222}  762  .772  \[ \{400}  277 \\ \{400}  277 \\ \{232}  762  .772  \[ \{400}  277 \\ \{400}  277 \\ \{215}  polyA_ site \{222}  762  .772  \[ \{400}  277 \\ \{400}  277 \\ \{215}  cotttagttct tttattgcta ggagaatgta gcaatagaag ttctcatcgc cctgtattgc acttttggtt ttaaggactg gaccaagagt tcctcaaaagc caaactccat aagctgtggg ctttgcta gtaagattca acacaatagc cggctkhagg atgcaatag gtcgaaggggg gttggtaaggttggtagagtcagtcagtggtcagtggtcagtggtcagtggtcagtggtggtggtggtagagggagg		467
tcaacctctt ctgaraaaaa aaattattc tgaggccaac tgttgctaca aaacaaattc tgactgaatg gttaaaact ttctagtara aggggaaaaa aaakttaaac atgcactgtt tgtgtgtata sccatttcat taaatataca gtaaaactyc aaaaaaaaaaa aa		
tgattgaatg gttaaaacat ttctagtara aggggaaaaa aaakttaaac atgcactgtt tgtgtgtata sccattcat taaatataca gtaaaactyc aaaaaaaaaa aa 639 <pre></pre>		527
tgtgtgtata sccattcat taaatataca gtaaaactyc aaaaaaaaaa aa 639 <pre> &lt;210&gt; 277 &lt;211&gt; 772 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  <pre> &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 284463 </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 284379 &lt;223&gt; Von Heijne matrix</pre></pre>	tractgaatg gttaaaacat ttctagtara aggggaaaaa aaakttaaac atgcactgtt	587
<pre> \( \frac{2}{2} \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \\ \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \\ \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \\ \ \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \\ \\ \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \\ \\ \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \\ \\ \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \( \) \</pre>	tgtgtgtata sccatttcat taaatataca gtaaaactyc aaaaaaaaaa aa	639
<pre> &lt;210&gt; 277 &lt;211&gt; 772 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;221&gt; CDS &lt;222&gt; 284463 </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 284379 &lt;223&gt; Von Heijne matrix</pre>		
<pre> &lt;210&gt; 277 &lt;211&gt; 772 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;221&gt; CDS &lt;221&gt; Sig_peptide &lt;222&gt; 284463 </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 284379 &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;211&gt; 772</pre>		
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;221&gt; CDS &lt;222&gt; 284463  &lt;221&gt; sig_peptide &lt;222&gt; 284379 &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 284463  &lt;221&gt; sig_peptide &lt;222&gt; 284379  &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;221&gt; CDS &lt;222&gt; 284463  &lt;221&gt; sig_peptide &lt;222&gt; 284379 &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;221&gt; CDS &lt;222&gt; 284463  &lt;221&gt; sig_peptide &lt;222&gt; 284379 &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;222&gt; 284463  &lt;221&gt; sig_peptide &lt;222&gt; 284379 &lt;223&gt; Von Heijne matrix</pre>		·
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 284379 &lt;223&gt; Von Heijne matrix</pre>		
<pre>&lt;222&gt; 284379 &lt;223&gt; Von Heijne matrix</pre>	(222) 201403	
<pre>&lt;223&gt; Von Heijne matrix</pre>	<221> sig_peptide	
score 3.79999995231628 seq TFINITLWLGSLC/QR  <221> polyA_site <222> 762772  <400> 277 acagctgggg ctttgtcttc tttattgcta ggagaatgta gcaatagaag ttctcatcgc ctgtattgc acttttggtt ttaaggactg gacccagagt tcctgaaagc caaactccat 120 aagctgctca gtaagttcca agcacatagc cggctkhggg atgcgattcg gtcgaggtct gttgaatgaa ggtagacgca gcaggcagtt tgtccttacc agtgacctgg aagacggtgg 240 cacttcctga gtgagctcac ttaccttccc tgaatggtga ggc atg gat gaa tat 295  **Met Asp Glu Tyr** -30  tcc tgg tgg tgc cac gtg tta gag gtg gta aag ggt caa atg ttt act 343 Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr -25 -20 -15  ttt att aat att aca tta tgg ctt ggt tct ctg tgt cag cga ttt tc 391 Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe -10 -5 1 tat gcc tcg ggt act tat ttc cta ata tat act agc aca gta acg cct 439 Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro 5 10 15 20 agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg Ser Trp Arg Leu Cys Leu Val Ser -25  ttacctcca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct tttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt 633 acagatgtgt tgattttaaa gtgggtatag ggcctgagcc ctggagtttg agaccaccg 733		
<pre></pre>		
<pre>&lt;221&gt; polyA_site &lt;222&gt; 762772  &lt;400&gt; 277 acagctgggg ctttgtcttc tttattgcta ggagaatgta gcaatagaag ttctcatcgc ctgtattgc acttttggtt ttaaggactg gaccagagt tcctgaaagc caaactccat 120 aagctgctca gtaagttcca agcacatage cggctkhggg atgcgattcg gtcgaggtct 180 gttgaatgaa ggtagacgca gcaggcagtt tgtccttacc agtgacctgg aagacggtgg 240 cacttcctga gtgagctcac ttaccttccc tgaatggtga ggc atg gat gaa tat 295</pre>		
<pre>&lt;400&gt; 277 acagctgggg ctttgtcttc tttattgcta ggagaatgta gcaatagaag ttctcatcgc cctgtattgc acttttggtt ttaaggactg gacccagagt tcctgaaagc caaactccat aagctgctca gtaagttcca agcacatagc cggctkhggg atgcgattcg gtcgaggtct gttgaatgaa ggtagacgca gcaggcagtt tgtccttacc agtgacctgg aagacggtgg cacttcctga gtgagctcac ttaccttccc tgaatggtga ggc atg gat gaa tat</pre>	sed itiminappe, 6%	
<pre>&lt;400&gt; 277 acagctgggg ctttgtcttc tttattgcta ggagaatgta gcaatagaag ttctcatcgc cctgtattgc acttttggtt ttaatggactg gacccagagt tcctgaaagc caaactccat aagctgctca gtaagttcca agcacatagc cggctkhggg atgcgattcg gtcgaggtct gttgaatgaa ggtagacgca gcaggcagtt tgtccttacc agtgacctgg aagacggtgg cacttcctga gtgagctcac ttaccttccc tgaatggtga ggc atg gat gaa tat</pre>	<221> polyA_site	
acagetgggg ctttgtette tttattgeta ggagaatgta geaatagaag tteteatege cettgtattge acttttggtt ttaaggactg gacceagagt teetgaaage caaactecat 120 aagetgetea gtaagtteea ageacatage eggetkhggg atgegatteeg gtegaggtet 180 gttgaatgaa ggtagaegea geaggeagtt tgteettace agtgaectgg aagaeggtgg 240 caetteetga gtgageteae ttaeetteee tgaatggtga gge atg gat gaa tat 295 Met Asp Glu Tyr -30 tee tgg tgg tge cae gtg tta gag gtg gta aag ggt caa atg ttt act 343 Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr -25 -20 -15 ttt att aat att aca tta tgg ett ggt tee cys Gln Arg Phe Phe -10 -5 1 tat gee teg ggt act tat tte cta ata tat ace age aca gta acg ect 439 Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro 10 age tgg agg ett tgt ett gtt gataaatta gtggtaacag gtagatttgg 493 Ser Trp Arg Leu Cys Leu Val Ser 25 ttaeeteea aagtgetgg attreagaeg tgagecaecg egeetggeeg aaacaattet ttgaaagag agaagtetee ettgtttgeeg eaggetggte teagaeteet ggggteaagt gageeteetg ettetegeete ctaaagtget gggattacag gegtgageea cegeaeceg aaagatgtgt tgatttaaa gtgggtatga ggeettgggeete etgagaeteeg aaaagaegeet 733 acagattgt tgattttaaa gtgggtatga ggeettgagee etggagettg agaecaegeet 733	<222> 762772	
acagetgggg ctttgtette tttattgeta ggagaatgta geaatagaag tteteatege cettgtattge acttttggtt ttaaggactg gacceagagt teetgaaage caaactecat 120 aagetgetea gtaagtteea ageacatage eggetkhggg atgegatteeg gtegaggtet 180 gttgaatgaa ggtagaegea geaggeagtt tgteettace agtgaectgg aagaeggtgg 240 caetteetga gtgageteae ttaeetteee tgaatggtga gge atg gat gaa tat 295 Met Asp Glu Tyr -30 tee tgg tgg tge cae gtg tta gag gtg gta aag ggt caa atg ttt act 343 Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr -25 -20 -15 ttt att aat att aca tta tgg ett ggt tee cys Gln Arg Phe Phe -10 -5 1 tat gee teg ggt act tat tte cta ata tat ace age aca gta acg ect 439 Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro 10 age tgg agg ett tgt ett gtt gataaatta gtggtaacag gtagatttgg 493 Ser Trp Arg Leu Cys Leu Val Ser 25 ttaeeteea aagtgetgg attreagaeg tgagecaecg egeetggeeg aaacaattet ttgaaagag agaagtetee ettgtttgeeg eaggetggte teagaeteet ggggteaagt gageeteetg ettetegeete ctaaagtget gggattacag gegtgageea cegeaeceg aaagatgtgt tgatttaaa gtgggtatga ggeettgggeete etgagaeteeg aaaagaegeet 733 acagattgt tgattttaaa gtgggtatga ggeettgagee etggagettg agaecaegeet 733		
cctgtattgc acttttggtt ttaaggactg gacccagagt tcctgaaagc caaactccat aagctgctca gtaagttcca agcacatagc cggctkhggg atgcgattcg gtcgaggtct gttgaatgaa ggtagacgca gcaggcagtt tgtccttacc agtgacctgg aagacggtgg cacttcctga gtgagctcac ttaccttccc tgaatggtga ggc atg gat gaa tat  Met Asp Glu Tyr  -30  tcc tgg tgg tgc cac gtg tta gag gtg gta aag ggt caa atg ttt act Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr  -25  -20  -15  ttt att aat att aca tta tgg ctt ggt tct ctg tgt cag cga ttt ttc Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe  -10  -5  1  tat gcc tcg ggt act tat ttc cta ata tat atc agc aca gta acg cct Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro 5  10  15  20  agc tgg agg ctt tgt ct gtt agt tgataaatta gtggtaacag gtagatttgg Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct tttgaaagag agaagtctc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg acagatggt tgatttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagct 733		60
aagetgetea gtaagtteca ageacatage eggetkhggg atgegatteg gtegaggtet gttgaatgaa ggtagaegea geaggeagtt tgteettace agtgaeeteg aagaeeggtgg cactteetga gtgageteae ttaeetteee tgaatggta gge atg gat gaa tat  Met Asp Glu Tyr  -30  tee tgg tgg tge cae gtg tta gag gtg gta aag ggt caa atg ttt act Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr  -25  -20  -15  ttt att aat att aca tta tgg ett ggt tee cag ega ttt tte Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe  -10  -5  tat gee teg ggt act tat tte eta ata tat ate age aca gta acg eet Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro  10  15  20  age tgg agg ett tgt ett gtt agt tgataaatta gtggtaacag gtagatttgg Ser Trp Arg Leu Cys Leu Val Ser  25  ttaeeteea aagtgetggg attreagaeg tgageeaceg egeetggeg aaacaattet tttgaaagag agaagtetee ettgtgttgeg eaggetggte teagaeteet ggggteaagt gageeteetg etttegeete ettaaagtget gggattaeag gegtgageea eeggeaece	cctgtattgc acttttggtt ttaaggactg gacccagagt tcctgaaagc caaactccat	120
cacttcctga gtgagctcac ttaccttccc tgaatggtga ggc atg gat gaa tat  Met Asp Glu Tyr  -30  tcc tgg tgg tgc cac gtg tta gag gtg gta aag ggt caa atg ttt act  Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr  -25  ttt att aat att aca tta tgg ctt ggt tct ctg tgt cag cga ttt ttc  Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe  -10  -5  tat gcc tcg ggt act tat ttc cta ata tat atc agc aca gta acg cct  Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro  5  10  15  agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg  Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct  tttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt  gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg  acagatgtgt tgatttaaa gtgggtatga ggcctgagcc ctggagtttg agaccaccc  733	aagctgctca gtaagttcca agcacatage eggetkhggg atgegatteg gtegaggtet	_
tcc tgg tgg tgc cac gtg tta gag gtg gta aag ggt caa atg ttt act  Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr  -25  ttt att aat att aca tta tgg ctt ggt tct ctg tgt cag cga ttt ttc  Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe  -10  tat gcc tcg ggt act tat ttc cta ata tat atc agc aca gta acg cct  Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro  10  agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg  Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcaccgg  acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccaccc  733	qttqaatqaa ggtagacgca gcaggcagtt tgtccttacc agtgacctgg aagacggtgg	
tcc tgg tgg tgc cac gtg tta gag gtg gta aag ggt caa atg ttt act  Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr  -25  ttt att aat att aca tta tgg ctt ggt tct ctg tgt cag cga ttt ttc  Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe  -10  tat gcc tcg ggt act tat ttc cta ata tat atc agc aca gta acg cct  Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro  1  agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg  Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctcca aagtgctggg attrcagacg tgagccaccg cgcctggcg aaacaattct  ttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt  gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg  acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct  733	cactteetga gtgageteae ttacetteee tgaatggtga gge atg gat gaa tat	295
tcc tgg tgg tgc cac gtg tta gag gtg gta aag ggt caa atg ttt act  Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr  -25  ttt att aat att aca tta tgg ctt ggt tct ctg tgt cag cga ttt ttc  Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe  -10  tat gcc tcg ggt act tat ttc cta ata tat atc agc aca gta acg cct  Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro  10  15  20  agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg  Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct  ttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt  gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg  acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct  733		
Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr  -25  -20  -15  ttt att aat att aca tta tgg ctt ggt tct ctg tgt cag cga ttt ttc 391  Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe  -10  -5  tat gcc tcg ggt act tat ttc cta ata tat atc agc aca gta acg cct 439  Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro  5  10  15  20  agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg 493  Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct 553  tttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt 613  gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg 673  acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct 733	· · · · · · · · · · · · · · · · · · ·	343
ttt att aat att aca tta tgg ctt ggt tct ctg tgt cag cga ttt ttc 391  Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe  -10 -5 1  tat gcc tcg ggt act tat ttc cta ata tat atc agc aca gta acg cct 439  Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro  10 15 20  agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg 493  Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct tttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt 613  gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg 673  acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccacct 733	Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly Gln Met Phe Thr	
Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys Gln Arg Phe Phe  -10 -5 1  tat gcc tcg ggt act tat ttc cta ata tat atc agc aca gta acg cct 439  Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro 5 10 15 20  agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg 493  Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct 553  tttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt 613  gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg 673  acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct 733	-25 -20 -15	
tat gcc tcg ggt act tat ttc cta ata tat atc agc aca gta acg cct  Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro  10 15 20  agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg  Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct  ttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt  gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg  acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct  733  25	ttt att aat att aca tta tgg ctt ggt tct ctg tgt cag cga ttt ttc	391
tat gcc tcg ggt act tat ttc cta ata tat atc agc aca gta acg cct  Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro  5	_	
Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro 5 10 15 20  agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg 493  Ser Trp Arg Leu Cys Leu Val Ser 25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct 553  tttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt 613  gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg 673  acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct 733	-10	439
agc tgg agg ctt tgt ctt gtt agt tgataaatta gtggtaacag gtagatttgg 493 Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct 553 tttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt 613 gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg 673 acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct 733	Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser Thr Val Thr Pro	
Ser Trp Arg Leu Cys Leu Val Ser  25  ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct 553  tttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt 613  gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg 673  acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct 733	5 10 15 20	
ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct 553 tttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt 613 gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg 673 acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct 733		493
ttacctccca aagtgctggg attrcagacg tgagccaccg cgcctggccg aaacaattct 553 tttgaaagag agaagtctcc ctgtgttgcg caggctggtc tcagactcct ggggtcaagt 613 gagcctcctg ctttcgcctc ctaaagtgct gggattacag gcgtgagcca ccgcacccgg 673 acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct 733		
tttgaaagag agaagtetee etgtgttgeg eaggetggte teagacteet ggggteaagt 613 gageeteetg etttegeete etaaagtget gggattaeag gegtgageea eegeaceegg 673 acagatgtgt tgattttaaa gtgggtatga ggeetgagee etggagtttg agaceageet 733		553
gagcetectg etttegeete etaaagtget gggattacag gegtgageea eegeaceegg 673 acagatgtgt tgattttaaa gtgggtatga ggeetgagee etggagtttg agaceageet 733	tttgaaagag agaagtetee etgtgttgeg caggetggte teagacteet ggggtcaagt	
acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct 733	gageeteetg etttegeete etaaagtget gggattacag gegtgageea eegeaceegg	
ggacaacatg gcaagaccct gtctctccaa aaaaaaaaa 772	acagatgtgt tgattttaaa gtgggtatga ggcctgagcc ctggagtttg agaccagcct	
	ggacaacatg gcaagaccct gtctctccaa aaaaaaaaa	772

<sup>&</sup>lt;210> 278

<sup>&</sup>lt;211> 840

<sup>&</sup>lt;212> DNA

<213> Homo sapiens <220> <221> CDS <222> 162..671 <221> sig\_peptide <222> 162..398 <223> Von Heijne matrix score 4.09999990463257 seq QGVLFICFTCARS/FP <221> polyA\_signal <222> 805..810 <221> polyA\_site <222> 830..840 <400> 278 60 aaaaactgag gcctgggagc aggaacctgt aggcagcgct tgagggtagc gggatagcag ctgcaacgcg cgtgggaggc gggggctctg ggcggaacaa aaatcacagg atgtcagagg 120 atgtttcccg ggaagaactg ggataaaggg gtcccagcac c atg. gag gac ccg aac 176 Met Glu Asp Pro Asn cct gaa gag aac atg aag cag cag gat tca ccc aag gag aga agt ccc 224 Pro Glu Glu Asn Met Lys Gln Gln Asp Ser Pro Lys Glu Arg Ser Pro -65 cag age cca gga gge aac ate tge cae etg ggg gee eeg aag tge ace 272 Gln Ser Pro Gly Gly Asn Ile Cys His Leu Gly Ala Pro Lys Cys Thr -55 -50 320 cgc tgc ctc atc acc ttc gca gat tcc aag ttc cag gag cgt cac atg Arg Cys Leu Ile Thr Phe Ala Asp Ser Lys Phe Gln Glu Arg His Met -35 -30 aag cgg gag cac cca gcg gac ttc gtg gcc cag aag ctg cag ggg gtc 368 Lys Arg Glu His Pro Ala Asp Phe Val Ala Gln Lys Leu Gln Gly Val -20 -15 ctc ttc atc tgc ttc acc tgc gcc cgc tcc ttc ccc tcc tcc aaa gcc 416 Leu Phe Ile Cys Phe Thr Cys Ala Arg Ser Phe Pro Ser Ser Lys Ala -5 1 464 ckr rkc acc cac car cgc agc cac ggt cca rcc gcc aag ccc acc ctg Xaa Xaa Thr His Gln Arg Ser His Gly Pro Xaa Ala Lys Pro Thr Leu 15 512 ccg gtt gca acc act act gcc car ccc acc ttc cct tgt cct gac tgt Pro Val Ala Thr Thr Thr Ala Gln Pro Thr Phe Pro Cys Pro Asp Cys 25 30 560 ggc aaa acc ttt ggg cag gct gtt tct ctg arg cgg cac csc caa atr Gly Lys Thr Phe Gly Gln Ala Val Ser Leu Xaa Arg His Xaa Gln Xaa 45 608 cat gar gtc cgt gcc cct cct ggc acc ttc gcc tgc aca rad tgc ggt His Glu Val Arg Ala Pro Pro Gly Thr Phe Ala Cys Thr Xaa Cys Gly 60 65 cag gac ttt gct car gaa rca ggg ctg cat caa cac tac att cgg cat 656 Gln Asp Phe Ala Gln Glu Xaa Gly Leu His Gln His Tyr Ile Arg His 80 75 gcc cgg ggg gga ctc tgagttcagc ttaagcctct ccacggtgac gggtggctct 711 Ala Arg Gly Gly Leu gtggctggta ggactcaccc atgatatggg gtgcaggaac tctggggggcc ctgaaggatt 771 tgcttccctc ccctgggaag gcagagggct cttaataaag aggacccaka agattcttaa 831 840 aaaaaaaa

```
<210> 279
<211> 840
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 63..632
<221> sig_peptide
<222> 63..308
<223> Von Heijne matrix
      score 4.40000009536743
      seq NLPHLQVVGLTWG/HI
<221> polyA_signal
<222> 808..813
<221> polyA_site
<222> 829..840 .
<400> 279
aacttccggt cgcgccascg cccgttgcca gttctgcgcg tgtcctgcat ctccagtatg
                                                                       60
ga atg tat gtd tgg ccc tgt gct gtg gtc ctg gcc cag tac ctt tgg
                                                                      107
   Met Tyr Val Trp Pro Cys Ala Val Val Leu Ala Gln Tyr Leu Trp
                                -75
            -80
 ttt cac aga aga tct ctg cca ggc aag gcc atc tta gag att gga gct
                                                                       155
Phe His Arg Arg Ser Leu Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala
                                                 -55
                             -60
 gga gtg agc ctt cca gga att ttg gct gcc aaa tgt ggt gca gaa gta
                                                                       203
 Gly Val Ser Leu Pro Gly Ile Leu Ala Ala Lys Cys Gly Ala Glu Val
     -50
 ata ctg tca gac agc tca gaa ctg cct cac tgt ctg gaa gtc tgt cgg
                                                                       251
 Ile Leu Ser Asp Ser Ser Glu Leu Pro His Cys Leu Glu Val Cys Arg
                                         -25
                     -30
                                                                       299
 caa agc tgc caa atg aat aac ctg cca cat ctg cag gtg gta gga cta
 Gln Ser Cys Gln Met Asn Asn Leu Pro His Leu Gln Val Val Gly Leu
                  -15
 aca tgg ggt cat ata tct tgg gat ctt ctg gct cta cca cca caa gat
                                                                       347
 Thr Trp Gly His Ile Ser Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp
                                                                       395
 att atc ctt gca tct gat gtg ttc ttt gaa cca gaa rat ttt gaa gac
 Ile Ile Leu Ala Ser Asp Val Phe Phe Glu Pro Glu Xaa Phe Glu Asp
                          20
 att ttg gct aca ata tat ttt ttg atg cac aar aat ccc aag gtc caa
                                                                        443
 Ile Leu Ala Thr Ile Tyr Phe Leu Met His Lys Asn Pro Lys Val Gln
                                          40
                      35
  ttg tgg tct act tat caa gtt agg art gct gac tgg tca ctt gaa gct
                                                                        491
  Leu Trp Ser Thr Tyr Gln Val Arg Xaa Ala Asp Trp Ser Leu Glu Ala
                                      55
  tta ctc tac aaa tgg gat atg aaa tgt gtc cac att cct ctt gag tct
                                                                        539
  Leu Leu Tyr Lys Trp Asp Met Lys Cys Val His Ile Pro Leu Glu Ser
                                  70
  ttt gat gca gac aaa gaa rat ata gca gaa tct acc ctt cca gga aga
                                                                        587
  Phe Asp Ala Asp Lys Glu Xaa Ile Ala Glu Ser Thr Leu Pro Gly Arg
                              85
  cat aca gtt gaa atg ctg gtc att tcc ttt gca aag gac agt ctc
                                                                        632
  His Thr Val Glu Met Leu Val Ile Ser Phe Ala Lys Asp Ser Leu
                           100
  tgaattatac ctacaacctg ttctgggaca gtatcaatac tgatgagcaa cctggcacac
                                                                         692
  aaactatgag cagaccactt cagcttgaga atgcagtggg tctgaagatg gtcaagtctg
                                                                         752
```

tttgccttar attitgatgt cacctagaca acacttaaac tcatatgaaa caaaaattaa aatacgtatt acaadcaaaa aaaaaaaa 840 <210> 280 <211> 849 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 21..362 <221> sig\_peptide <222> 21..200 <223> Von Heijne matrix score 4.80000019073486 seq LVILSLKSQTLDA/ET <221> polyA signal <222> 821..826 <221> polyA site <222> 838..849 <400> 280 agtaagtccc cccgcctcgc atg atg gct gcg gtg ccg ccg ggc ctg gag ccg 53 Met Met Ala Ala Val Pro Pro Gly Leu Glu Pro -55 tgg aac cgt gtg aga atc cct aag gcg ggg aac cgc agc gca gtg aca 101 Trp Asn Arg Val Arg Ile Pro Lys Ala Gly Asn Arg Ser Ala Val Thr , -40 -45 gtg cag aac ccc ggc gcg gcc ctt gac ctt tgc att gca gct gta att 149 Val Gln Asn Pro Gly Ala Ala Leu Asp Leu Cys Ile Ala Ala Val Ile -25 aaa gaa tgc cat ctc gtc ata ctg tcg ctg aag agc caa acc tta gat 197 Lys Glu Cys His Leu Val Ile Leu Ser Leu Lys Ser Gln Thr Leu Asp -15 -10 -5 gca gaa aca gat gtg tta tgt gca gtc ctt tac agc aat cac aac aga 245 Ala Glu Thr Asp Val Leu Cys Ala Val Leu Tyr Ser Asn His Asn Arg 10 atg ggc cgc cac aaa ccc cat ttg gcc ctc aaa cag gtt gag caa tgt 293 Met Gly Arg His Lys Pro His Leu Ala Leu Lys Gln Val Glu Gln Cys 20 25 tta aag cgt ttg aaa aac atg aat ttg gag ggc tca att caa gac ctg 341 Leu Lys Arg Leu Lys Asn Met Asn Leu Glu Gly Ser Ile Gln Asp Leu . 35 40 ttt gag ttg ttt tct tcc aag taagtaagtg gtccarttgc tttgtgatgt 392 Phe Glu Leu Phe Ser Ser Lys ggtgggctgg gaactcaatg tettgtgate keeettwgga ttketetakg etygekgttg gaatataacc aattataccw cagctgtaka aatwitgtit taatgtgggg taccyggtgt 512 ktgtggtaat cttctgacat tgatctatgg gartgactgg tgtgacattg aaatctgggt 572 catggtagat tatattaaaa catcagtggg ctgttattgt gcttaactac ctcaagttga 632 gcttaaagca agtcttcact tgaaaactgc tatagaaatg ctttatattt aaaaatgaaa 692 gtaatgggar mttgcacata gctgaaaatg tgaagggtcg cccagggagg amatggaagc 752 tetgtgette ttetgecata cettgeceta tgeatetett tgttteaate etttgteata 812 tcctttataa taaactggta aatgtaaaaa aaaaaaa 849

```
<211> 1344
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 21..503
<221> sig_peptide
<222> 21..344
<223> Von Heijne matrix
      score 5.30000019073486
     seq ACMTLTASPGVFP/SL
<221> polyA_signal
<222> 1305.,1310
<221> polyA site
<222> 1330..1341
<400> 281
aaacaactcc ggaaagtaca atg acc agc ggg cag gcc cga gct tcc wyc cag
                      Met Thr Ser Gly Gln Ala Arg Ala Ser Xaa Gln
                                   -105
tcc ccc cag gcc ctg gag gac tcg ggc ccg gtg aat atc tca gtc tca
                                                                      101
Ser Pro Gln Ala Leu Glu Asp Ser Gly Pro Val Asn Ile Ser Val Ser
        -95
                            -90
                                                -85
atc acc cta acc ctg gac cca ctg aaa ccc ttc gga ggg tat tcc cgc
Ile Thr Leu Thr Leu Asp Pro Leu Lys Pro Phe Gly Gly Tyr Ser Arg
    -80
                        -75
aac gtc acc cat ctg tac tca acc atc tta ggg cat cag att gga ctt
                                                                      197
Asn Val Thr His Leu Tyr Ser Thr Ile Leu Gly His Gln Ile Gly Leu
                    -60
                                        -55
tca ggc agg gaa gcc cac gag gag ata aac atc acc ttc acc ctg cct
                                                                      245
Ser Gly Arg Glu Ala His Glu Glu Ile Asn Ile Thr Phe Thr Leu Pro
                -45
                                     -40
aca gcg tgg agc tca gat gac tgc gcc ctc cac ggt cac tgt gag cag
                                                                      293
Thr Ala Trp Ser Ser Asp Asp Cys Ala Leu His Gly His Cys Glu Gln
                                 -25
gtg gta ttc aca gcc tgc atg acc ctc acg gcc agc cct ggg gtg ttc
                                                                      341
Val Val Phe Thr Ala Cys Met Thr Leu Thr Ala Ser Pro Gly Val Phe
        -15
                            -10
ccg tca ctg tac agc cac cgc act gtg ttc ctg aca cgt aca gca acg
                                                                      389
Pro Ser Leu Tyr Ser His Arg Thr Val Phe Leu Thr Arg Thr Ala Thr
                                         10
cca cgc tct ggt aca aga tct tca caa ctg cca gag atg cca aca caa
                                                                      437
Pro Arg Ser Gly Thr Arg Ser Ser Gln Leu Pro Glu Met Pro Thr Gln
                20
aat acg ccc aaa att aca atc ctt tct ggt gtt ata agg ggg cca ttg
                                                                      485
Asn Thr Pro Lys Ile Thr Ile Leu Ser Gly Val Ile Arg Gly Pro Leu
            35
                                 40
gaa aag tot atc atg oft taaatcocaa gottacagtg attgttccag
                                                                      533
Glu Lys Ser Ile Met Leu
atgatgaccg ttcattaata aatttgcatc tcatgcacac cagttacttc ctctttgtga
                                                                      593
tggtgataac aatgttttgc tatgctgtta tcaagggcag acctagcaaa ttgcgtcaga
                                                                      653
gcaatcctga attttgtccc gagaaggtgg ctttggctga agcctaattc cacagctcct
                                                                      713
tgttttttga gagagactga gagaaccata atccttgcct gctgaaccca gcctgggcct
                                                                      773
ggatgctctg tgaatacatt atcttgcgat gttgggttat tccagccaaa gacatttcaa
                                                                      833
gtgcctgtaa ctgatttgta catatttata aaaatctatt cagaaattgg tccaataatg
                                                                      893
cacgtgcttt gccctgggta cagccagagc ccttcaaccc caccttggac ttgaggacct
                                                                       953
```

acctgatggg acgtttccac gtgtctctag agaaggatce tggatctage tggtcacgac gatgtttca ccaaggtcac aggagcattg cgtcgctgat ggggttgaag tttggtttgg	1013 1073 1133 1193 1253 1313 1344
	•
<210> 282	
<211> 671 <212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS <222> 1201	
(2227 2118V2	•
<221> sig_peptide	
<222> 163	
<223> Von Heijne matrix score 5.09999990463257	•
seq LLLKIWLLQRPES/QE	
<221> polyA_signal	
<222> 637642	•
<221> polyA_site <222> 660671	
<400> 282	
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt	48
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu	48
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu -20 -15 -10	48 96
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu	
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  -10  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  10	96
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  -10  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg agg agg gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt	
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  5  10  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Yarg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val	96
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25	96
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  5  10  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Yarg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val	96 144
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25  ttg ttg agt ttt cac tct tct aat gca agg gtc tca cac tgt gaa cca  Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro 30  35  40	96 144 192
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25  ttg ttg agt ttt cac tct tct aat gca agg gtc tca cac tgt gaa cca  Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro	96 144
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  -10  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25  ttg ttg agt ttt cac tct tct aat gca agg gtc tca cac tgt gaa cca  Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro  30  35  40  ctt agg atg tgatcacttt caggtggcca ggaatgttga atgtctttgg  Leu Arg Met	96 144 192 241
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  -10  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25  ttg ttg agt ttt cac tct tct aat gca agg gtc tca cac tgt gaa cca  Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro  30  35  40  ctt agg atg tgatcacttt caggtggcca ggaatgttga atgtctttgg  Leu Arg Met  45  ctcagttcat ttaaaaaaaga tatctatttg aaagttctca rarttgtaca tatgtttcac	96 144 192 241
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  -10  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25  ttg ttg agt ttt cac tct tct aat gca agg gtc tca cac tgt gaa cca  Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro  30  35  40  ctt agg atg tgatcacttt caggtggcca ggaatgttga atgtctttgg  Leu Arg Met  45  ctcagttcat ttaaaaaaaga tatctatttg aaagttctca rarttgtaca tatgtttcac  agtacaggat ctgtacataa aagtttcttt cctaaaccat tcaccaagag ccaatatcta	96 144 192 241 301 361
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  -10  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25  ttg ttg agt ttt cac tct tct aat gca agg gtc tca cac tgt gaa cca  Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro  30  35  40  ctt agg atg tgatcacttt caggtggcca ggaatgttga atgtctttgg  Leu Arg Met  45  ctcagttcat ttaaaaaaga tatctatttg aaagttctca rarttgtaca tatgtttcac  agtacaggat ctgtacataa aagtttcttt cctaaaccat tcaccaagag ccaatatcta  ggcattttct tggtagcaca aatttctta ttgcttaraa aattgcctc cttgttattt	96 144 192 241 301 361 421
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  -10  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25  ttg ttg agt ttt cac tct tct aat gca agg gtc tca cac tgt gaa cca  Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro  30  35  40  ctt agg atg tgatcacttt caggtggcca ggaatgttga atgtctttgg  Leu Arg Met  45  ctcagttcat ttaaaaaaga tatctatttg aaagttctca rarttgtaca tatgttcac  agtacaggat ctgtacataa aagtttcttt cctaaaccat tcaccaagag ccaatatcta  ggcattttct tggtagcaca aattttctta ttgcttaraa aattgtcctc cttgttattt  ctgtttgtaa racttaagtg agttaggtct ttaaggaaag caacgctcct ctgaaatgct	96 144 192 241 301 361 421 481
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  -10  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25  ttg ttg agt ttt cac tct tct aat gca agg gtc tca cac tgt gaa cca  Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro  30  35  40  ctt agg atg tgatcacttt caggtggcca ggaatgttga atgtctttgg  Leu Arg Met  45  ctcagttcat ttaaaaaaga tatctatttg aaagttctca rarttgtaca tatgtttcac  agtacaggat ctgtacataa aagtttcttt cctaaaccat tcaccaagag ccaatatcta  ggcatttct tggtagcaca aattttctta ttgcttaraa aattgtcctc cttgttattt  ctgtttgtaa racttaagtg agttaggtct ttaaaggaaag caacgctcct ctgaaatgct  tgtcttttt ctgttgccga aatarctggt cctttttcgg gagttaratg tatarartgt	96 144 192 241 301 361 421 481 541
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  -10  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25  ttg ttg agt tt cac tct tct aat gca agg gtc tca cac tgt gaa cca  Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro  30  35  40  ctt agg atg tgatcacttt caggtggcca ggaatgttga atgtcttgg  Leu Arg Met  45  ctcagttcat ttaaaaaaga tatctatttg aaagttctca rarttgtaca tatgtttcac  agtacaggat ctgtacataa aagttcttt cctaaaccat tcaccaagag ccaatatcta  ggcatttct tggtagcaca aatttctta ttgcttaraa aattgtcctc cttgaaatgt  tctgtttgtaa racttaagtg agttaggtct ttaaggaaag caacgctcct ctgaaatgct  tgtcttttt ctgttgccga aatarctggt cctttttcgg gagttaratg tatarartgt  ttgtatgtaa acatttcttg taggcatcac catgaacaaa gatatttt ctatttattt	96 144 192 241 301 361 421 481 541 601
atg ctg gga ggt gac cat agg gct ctg ctt tta aag ata tgg ctg ctt  Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu  -20  -15  -10  caa agg cca gag tca cag gaa gga ctt ctt cca ggg aga tta gtg gtg  Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val  -5  1  atg gag agg aga gtt aaa aat gac ctc atg tcc ttc ttg tcc acg gtt  Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val  15  20  25  ttg ttg agt ttt cac tct tct aat gca agg gtc tca cac tgt gaa cca  Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro  30  35  40  ctt agg atg tgatcacttt caggtggcca ggaatgttga atgtctttgg  Leu Arg Met  45  ctcagttcat ttaaaaaaga tatctatttg aaagttctca rarttgtaca tatgtttcac  agtacaggat ctgtacataa aagtttcttt cctaaaccat tcaccaagag ccaatatcta  ggcatttct tggtagcaca aattttctta ttgcttaraa aattgtcctc cttgttattt  ctgtttgtaa racttaagtg agttaggtct ttaaaggaaag caacgctcct ctgaaatgct  tgtcttttt ctgttgccga aatarctggt cctttttcgg gagttaratg tatarartgt	96 144 192 241 301 361 421 481 541

<210> 283 <211> 1601 <212> DNA <213> Homo sapiens

<220> <221> CDS <222> 39..1034 <221> sig\_peptide <222> 39..134 <223> Von Heijne matrix score 6.09999990463257 seq LPLLTSALHGLQQ/QH <221> polyA\_signal <222> 1566..1571 <221> polyA\_site <222> 1587..1597 <400> 283 agececagat cetgaaggag gtgcagagee cagagggg atg ate keg etg agg gae Met Ile Xaa Leu Arg Asp aca gct gcc tcc ctc cgc ctt gag aga gac aca agg cag ttg cca ctg 104 Thr Ala Ala Ser Leu Arg Leu Glu Arg Asp Thr Arg Gln Leu Pro Leu -25 -20 -15 ctc acc agt gcc ctg cac gga ctg cag cag cac cca gcc ttc tct 152 Leu Thr Ser Ala Leu His Gly Leu Gln Gln His Pro Ala Phe Ser -5 ggt gtg gca cgg ctg gcc aag cgg tgg gtg cgt gcc cag ctt ctt ggt 200 Gly Val Ala Arg Leu Ala Lys Arg Trp Val Arg Ala Gln Leu Leu Gly 15 gag ggt ttc gct gat gag agc ctg gat ctg gtg gcc gct gcc ctt ttc 248 Glu Gly Phe Ala Asp Glu Ser Leu Asp Leu Val Ala Ala Ala Leu Phe ctg cac cct gag ccc ttc acc cct ccg agt tcc ccc cag gtt ggc ttc 296 Leu His Pro Glu Pro Phe Thr Pro Pro Ser Ser Pro Gln Val Gly Phe 45 ctt cga ttc ctt ttc ttg gta tca acg ttt gat tgg aag aac aac ccc 344 Leu Arg Phe Leu Phe Leu Val Ser Thr Phe Asp Trp Lys Asn Asn Pro 60 ctc ttt gtc aac ctc aat aat gag ctc act gtg gag gag cag gtg gar 392 Leu Phe Val Asn Leu Asn Asn Glu Leu Thr Val Glu Glu Gln Val Glu 80 ate ege agt gge tte etg gea get egg gea eag ete eee gte atg gte 440 Ile Arg Ser Gly Phe Leu Ala Ala Arg Ala Gln Leu Pro Val Met Val att gtt acc ccc caa rac cgc aaa aac tct gtg tgg aca cag gat gga 488 Ile Val Thr Pro Gln Xaa Arg Lys Asn Ser Val Trp Thr Gln Asp Gly 105 110 ccc tca gcc car atc ctg cag cag ctt gtg gtc ctg gca gct gaa scc 536 Pro Ser Ala Gln Ile Leu Gln Gln Leu Val Val Leu Ala Ala Glu Xaa 125 ctg ccc atg tta rar aas cag ctc atg gat ccc cgg gga cct ggg gac 584 Leu Pro Met Leu Xaa Xaa Gln Leu Met Asp Pro Arg Gly Pro Gly Asp 135 140 145 150 atc agg aca gkg ttc egg eeg eec ttg gae att tae gae gtg etg att 632 Ile Arg Thr Xaa Phe Arg Pro Pro Leu Asp Ile Tyr Asp Val Leu Ile 155 160 ege etg tet eet ege eat ate eeg egg eae ege eag get gtg gae ter 680 Arg Leu Ser Pro Arg His Ile Pro Arg His Arg Gln Ala Val Asp Ser 175 cca gct gcc tcc ttc tgc cgg ggc ctg ctc agc cag ccg ggg ccc tca 728

Pro Ala Ala Ser Phe Cys Arg Gly Leu Leu Ser Gln Pro Gly Pro Ser

185 <sup>t</sup> , 190 195	
tcc ctg atg ccc gtg ctg ggc tak gat cct cct cag ctc tat ctg acg	776
Ser Leu Met Pro Val Leu Gly Xaa Asp Pro Pro Gln Leu Tyr Leu Thr	
200 205 210	
cag ctc arg gag gcc ttt ggg gat ctg gcc ctt ttc ttc tat gac cag	824
Gln Leu Xaa Glu Ala Phe Gly Asp Leu Ala Leu Phe Phe Tyr Asp Gln	
215 220 225 230	
cat ggt gga gag gtg att ggt gtc ctc tgg aag ccc acc agc ttc cag	872
His Gly Gly Glu Val Ile Gly Val Leu Trp Lys Pro Thr Ser Phe Gln	
235 240 245	
ccg cag ccc ttc aag gcc tcc agc aca aag ggg cgc atg gtg atg tct	920
Pro Gln Pro Phe Lys Ala Ser Ser Thr Lys Gly Arg Met Val Met Ser	
250 255 260	
cga ggt ggg gag cta gta atg gtg ccc aat gtt gaa gca atc ctg gag	, 968
Arg Gly Glu Leu Val Met Val Pro Asn Val Glu Ala Ile Leu Glu	•
265 270 275	
gac ttt gct gtg ctg ggt gaa ggc ctg gtg cag act gtg gag gcc cga	1016
Asp Phe Ala Val Leu Gly Glu Gly Leu Val Gln Thr Val Glu Ala Arg	
280 285 290	
agt gag agg tgg act gtg tgatcccagc tctggagcaa gctgtagacg	1064
Ser Glu Arg Trp Thr Val	•
295 300	
gacagcagga cattggacct ctagagcaag atgtcagtag gatgacctcc accctccttg	1124
gacatgaatc ctccatggag ggcctgctgg ctgaacatgc tgaatcatct ccaacaaaac	1184
ccagccccaa ctttctctct gatgctccag cattggggca ggggcatggt ggcccatgta	1244
gtctcctggg cctcaccatc ccagaagagg agtgggagcc agctcagaga aggaactgaa	1304
cccaggagat ccatccacct attagecetg ggeetggace tecetgegat treccactee	1364
tttcttagtc ttcttccaga aacagagaag gggatgtgtg cctgggagag gctctgtctc	1424
cttcctgctg ccaggacctg tgcctagact tagcatgccc ttcactgcag tgtcaggcct	1484
ttagatggga cccagcgaaa atgtggccct tctgagtcac atcaccgaca ctgagcagtg	1544
gaaaggggct atatgtgtat gaatagacca cattgaagga gcaaaaaaaa aaamcch	1601
•	
<210> 284	
<211> 1206	
<212> DNA	
<213> Homo sapiens	•
<220>	
<221> CDS	
<222> 69263	
<221> sig_peptide	
<222> 69125	
<223> Von Heijne matrix	
score 3.9000009536743	
seq ALSMSSFSFHSSS/CS	
<221> polyA_signal	
<222> 11731178	
.000	
<221> polyA_site	
<222> 11961205	
-400004	
<400> 284	
acattigiga cittaccaat acceteccag tietigatag acagetgiag gitgetgggt	60
tcaagaat atg ggt ggg ata tgg aat gct ctt tca atg tct agc ttc agt	110
Met Gly Gly Ile Trp Asn Ala Leu Ser Met Ser Ser Phe Ser	
-15 -10	
ttt oot too too too too too oo oo oo oo	
ttt cat tca tcc tcc tgc tca gca ctg tca gcc aag agc tta ctc agc	158
ttt cat tca tcc tcc tgc tca gca ctg tca gcc aag agc tta ctc agc Phe His Ser Ser Ser Cys Ser Ala Leu Ser Ala Lys Ser Leu Leu Ser	158

-5 1 10 aga cac cac atã ctg cag cag ttc cta gtg aga aaa tct gtg cca cta	206 .
Arg His His Ile Leu Gln Gln Phe Leu Val Arg Lys Ser Val Pro Leu	
15 20 25	
gaa aat get tea ett eea ttt eet eac etg gge agt tet etg ttt aaa	254
Glu Asn Ala Ser Leu Pro Phe Pro His Leu Gly Ser Ser Leu Phe Lys	
30 35 40	
att gtg ggc tgatttggtc ttcctctcct cctcccactg ttactgccct	303
Ile Val Cly	•
45	
gcagcccttg ttcaggtgta cagaccctta ttctggcctc tagtgtcctt gtctgtcatg	363
acacaccett cegeceaaat acetetgace ceaaggetgg aatggggetg gtaggarata	423
agtitgctta ctcatartca tgtcctttct cttggcacct gcttccctgc ggtgtcctca	. 483
aatggatttc tgtgtggcag tggartgatt gcatgaattt ttctgtaaca cattaacttt	543
gtattattat taagggartt tgaraaagct ttgcttataa tgtcaaggca aggaggtaaa	. 603 .
aactggagcc caaakaaatt cccttagggc aagattatgt tataataraa aattgaattt	663
cctgaggcag tggctgccac cccttttcar atgtttagtc ctgcaaatag catctttctt	723
gtagtctgtg acatggatgg ggatgctagg gcccttaggg gcaaggggac taaactaaat	<sub>.</sub> 783
caakttgagt ttttttccag caggggttar gggaggtact csctgttgat atttgacact	843
araaagtaat cttttttaca aaactgtttt tctaggtggg tggaaagtga aactgccaca	903
tccttgttgg tttagtccaa raratcattt gcaacaacag taratgtccg ggttttgttt	963
ctgtcttttt attatgaaaa actatgttaa gggggaaaat gtggattatg gtaaccarag	1023
gaatccctas ccttgttttc cttaraarac ttgtttagtg ttttatcara cgtctgttgt	1083
agttgtarac aggaaagctt gtgaraaaaa caccacatgg ascctgtaaa tgtttttgca	1143
caacctgtaa agcattcttg gaaktggcca gtaaaaaggg gttttaccat ttaaaaaaaa	1203
aat	1206
·	
<210> 285	
<211> 536	
<212> DNA	
<212> DNA <213> Homo sapiens	
<212> DNA <213> Homo sapiens <220>	
<212> DNA <213> Homo sapiens <220> <221> CDS	
<212> DNA <213> Homo sapiens <220>	
<212> DNA <213> Homo sapiens <220> <221> CDS <222> 115285	
<212> DNA <213> Homo sapiens <220> <221> CDS <222> 115285 <221> sig_peptide	
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 115285  <221> sig_peptide <222> 115204	
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 115285  <221> sig_peptide <222> 115204 <223> Von Heijne matrix	
<212> DNA <213> Homo sapiens  <220> <221> CDS <222> 115285  <221> sig_peptide <222> 115204	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix score 3.70000004768372</pre>	·
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix score 3.70000004768372</pre>	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	60
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	60 117
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	-
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	-
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204  &lt;223&gt; Von Heijne matrix</pre>	117
<pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 115285  &lt;221&gt; sig_peptide &lt;222&gt; 115204 &lt;223&gt; Von Heijne matrix</pre>	117

Val Tyr His Tyr Phe Gln Trp Arg Arg Ala Gln Arg Gln Ala Ala Glu 5 10 15	
gaa cag aag dac tca gga atc atg tagaactggg gggctttttc tcctgagcar Glu Gln Lys Xaa Ser Gly Ile Met 20 25	315
asakgcccaa ggcatgctgt ggagagactt cacctgccac catttccagg tcaacaggac tagagcgttg atggtttca aaccctgttg gaagaaagtg cccatggttt ctctggttct gccartttga cagtttatgg argcttttga atcgtaatar caatgtgagg gtgargtaca cctacagaca ttaaataatt tgctgtgtca aaaaaaaaaa	375 435 495 536
<210> 286 <211> 529 <212> DNA <213> Homo sapiens	· ·
<220>	
<221> CDS <222> 90344	
<221> sig_peptide <222> 90140 <223> Von Heijne matrix score 8.19999980926514 seq LLLITAILAVAVG/FP	•
<221> polyA_signal <222> 500505	
<221> polyA_site <222> 515527	
<400> 286 aatatrarac agetacaata ttecagggee arteaettge cattteteat aacagegtea	60
gagagaaaga actgactgar acgtttgag atg aag aaa gtt ctc ctc ctg atc  Met Lys Val Leu Leu Leu Ile  -15	60 113
aca gcc atc ttg gca gtg gct gtw ggt ttc cca gtc tct caa gac cag Thr Ala Ile Leu Ala Val Ala Val Gly Phe Pro Val Ser Gln Asp Gln -5 1 5	161
gaa cga gaa aaa aga agt atc agt gac agc gat gaa tta gct tca ggr Glu Arg Glu Lys Arg Ser Ile Ser Asp Ser Asp Glu Leu Ala Ser Gly 10 15 20	209
wtt ttt gtg ttc cct tac cca tat cca ttt cgc cca ctt cca cca att Xaa Phe Val Phe Pro Tyr Pro Tyr Pro Phe Arg Pro Leu Pro Pro Ile 25 30 35	257
Pro Phe Pro Arg Phe Pro Trp Phe Arg Arg Asn Phe Pro Ile Pro Ile 40 45 50 55	305
cct gaa tct gcc cct aca act ccc ctt cct agc gaa aag taaacaaraa Pro Glu Ser Ala Pro Thr Thr Pro Leu Pro Ser Glu Lys 60 65	354
ggaaaagtca crataaacct ggtcacctga aattgaaatt gagccacttc cttgaaraat caaaattcct gttaataaaa raaaaacaaa tgtaattgaa atagcacaca gcattctcta gtcaatatct ttagtgatct tctttaataa acatgaaagc aaaaaaaaaa	414 474 529

<sup>&</sup>lt;210> 287

<sup>&</sup>lt;211> 493

<sup>&</sup>lt;212> DNA

```
<213> Homo sapiens
<220>
<221> CDS
<222> 57..311
<221> sig_peptide
<222> 57..107
<223> Von Heijne matrix
      score 8.19999980926514
      seg LLLITAILAVAVG/FP
<221> polyA_signal
<222> 467..472
<221> polyA_site
<222> 482..493
<400> 287
aacttgccat ttctcataac agcgtcagag agaaagaact gactgaaacg tttgag atg
                                                                       59
                                                               Met
                                                                      107
aag aaa gtt ctc ctc ctg atc aca gcc atc ttg gca gtg gct gtt ggt
Lys Lys Val Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val Gly
                         -10
                                             -5
                                                                      155
ttc cca gtc tct caa gac cak gaa cga gaa aaa aga agt atc agt gac
Phe Pro Val Ser Gln Asp Xaa Glu Arg Glu Lys Arg Ser Ile Ser Asp
                                                                      203
age gat gaa tta get tea ggg ttt ttt gtg tte eet tae eea tat eea
Ser Asp Glu Leu Ala Ser Gly Phe Phe Val Phe Pro Tyr Pro Tyr Pro
                                 25
             20
 ttt cgc cca ctt cca cca att cca ttt cca aga ttt cca tgg ttt aga
                                                                       251
 Phe Arg Pro Leu Pro Pro Ile Pro Phe Pro Arg Phe Pro Trp Phe Arg
         35
                             40
                                                 45
                                                                       299
 cgt aat ttt cct att cca ata cct gaa tct gcc cct aca act ccc ctt
Arg Asn Phe Pro Ile Pro Ile Pro Glu Ser Ala Pro Thr Thr Pro Leu
                         55
 ccg agc gaa aag taaacaagaa ggaaaagtca cgataaacct ggtcacctga
                                                                       351
 Pro Ser Glu Lys
 aattgaaatt gagccacttc cttgargaat caaaattcct gttaataaaa gaaaaacaaa
                                                                       411
 tgtaattgaa atagcacaca gcattctcta gtcaatatct ttagtgatct tctttaataa
                                                                       471
                                                                       493
 acatgaaagc aaaaaaaaa aa
 <210> 288
```

<211> 521 <212> DNA <213> Homo sapiens

<220>

<221> CDS

<222> 96..302

<221> sig\_peptide

<222> 96..182

<223> Von Heijne matrix score 5 seg ELSLLPSSLWVLA/TS

<221> polyA\_site <222> 501..514

aagagacgtc accggctgcg cccttcagta tcgcggacg	g aagatggegt eegeéaceeg 60
tctcatccag cggctgcgga actgggcgtc cgggc atg	acc tgc agg gga agc 113
Met	Thr Cys Arg Gly Ser
	-25
tgc agc tac gct acc agg aga tct cca agc ga	a ctc agc ctc ctc cca 161
Cys Ser Tyr Ala Thr Arg Arg Ser Pro Ser Gl	
-20 -15	-10
<del></del> _	<del>-</del> -
age tee etg tgg gte eta gee aca age tet ee	
Ser Ser Leu Trp Val Leu Ala Thr Ser Ser Pr	o Thr lie Thr lie Ala
-5 <u>1</u>	5
ctc gcg atg gcc gcc ggg aat ctg tgc ccc ct	t cca tca tca tkt cgt 257
Leu Ala Met Ala Ala Gly Asn Leu Cys Pro Le	u Pro Ser Ser Xaa Arg
10 15 20	25
crc aaa agg cgc tgg tgt cag gca asc car ca	a ara gct ctg ctg 302
Xaa Lys Arg Arg Trp Cys Gln Ala Xaa Gln Gl	
30 35	40
tagctgccac tgaaaaraag gcggtgactc cagctcctc	
cctcggacca gccttacctg tgacactgca ccctcacgg	
ttggatttcc tccagggaga atgtgaccta atttatgac	a aatacgtara gctcaggtat 482
cacttctagt tttactttaa aaaataaaaa aatagagac	521
<210> 289	
<211> 811	
<212> DNA	•
<213> Homo sapiens	
•	
<220>	
<221> CDS	
<222> 161526	
<221> sig_peptide	
<222> 161328	
<223> Von Heijne matrix	
score 4.19999980926514	•
GOG VEDITEINITOOO/CI	
seq XSPLLTLALLGQC/SL	
sed vs.nninwnne&c\sn	
<pre>&lt;221&gt; polyA site</pre>	
•	
<221> polyA_site	
<221> polyA_site <222> 799811	
<221> polyA_site <222> 799811 <400> 289	o tatogataga 222gataga 60
<221> polyA_site <222> 799811 <400> 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg	
<221> polyA_site <222> 799811  <400> 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc	t gcactgctct ggtctagtac 120
<221> polyA_site <222> 799811 <400> 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175
<221> polyA_site <222> 799811  <400> 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc	t gcactgctct ggtctagtac 120
<221> polyA_site <222> 799811  <400> 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175
<221> polyA_site <222> 799811 <400> 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55
<221> polyA_site <222> 799811  <400> 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart agg ggc aag gtg aaa act gct cct att ccc at	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223
<221> polyA_site <222> 799811  <400> 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg tcctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe
<221> polyA_site <222> 799811  <400> 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg tcctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il -50 -45	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40
<221> polyA_site <222> 799811  <400> 289  aaaaaattgc agtgctgaag acactggacc cgcaaaagg tcctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il  -50  -45 ctc cct acc cac gac cca ccc acc cca gca ca	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40 t tgg tct cca gca tct 271
<221> polyA_site <222> 799811  <400> 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il -50 -45 ctc cct acc cac gac cca ccc acc cca gca ca Leu Pro Thr His Asp Pro Pro Thr Pro Ala Hi	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40 t tgg tct cca gca tct 271 s Trp Ser Pro Ala Ser
<pre>&lt;221&gt; polyA_site &lt;222&gt; 799811  &lt;400&gt; 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il</pre>	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40 t tgg tct cca gca tct 271 s Trp Ser Pro Ala Ser 5 -20
<pre>&lt;221&gt; polyA_site &lt;222&gt; 799811  &lt;400&gt; 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il</pre>	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40 t tgg tct cca gca tct 271 s Trp Ser Pro Ala Ser 5 -20 c act ttg gcc ctg ctg 319
<pre>&lt;221&gt; polyA_site &lt;222&gt; 799811  &lt;400&gt; 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il</pre>	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40 t tgg tct cca gca tct 271 s Trp Ser Pro Ala Ser 5 -20 c act ttg gcc ctg ctg 319
<pre>&lt;221&gt; polyA_site &lt;222&gt; 799811  &lt;400&gt; 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il</pre>	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40 t tgg tct cca gca tct 271 s Trp Ser Pro Ala Ser 5 -20 c act ttg gcc ctg ctg 319
<pre>&lt;221&gt; polyA_site &lt;222&gt; 799811  &lt;400&gt; 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il</pre>	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40 t tgg tct cca gca tct 271 s Trp Ser Pro Ala Ser 5 -20 c act ttg gcc ctg ctg 319 u Thr Leu Ala Leu Leu -5
<pre>&lt;221&gt; polyA_site &lt;222&gt; 799811  &lt;400&gt; 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il</pre>	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40 t tgg tct cca gca tct 271 s Trp Ser Pro Ala Ser 5 -20 c act ttg gcc ctg ctg 319 u Thr Leu Ala Leu Leu -5 a aaa ctt gca ggg caa 367
<pre>&lt;221&gt; polyA_site &lt;222&gt; 799811  &lt;400&gt; 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il</pre>	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40 t tgg tct cca gca tct 271 s Trp Ser Pro Ala Ser 5 -20 c act ttg gcc ctg ctg 319 u Thr Leu Ala Leu Leu -5 a aaa ctt gca ggg caa 367 s Lys Leu Ala Gly Gln
<pre>&lt;221&gt; polyA_site &lt;222&gt; 799811  &lt;400&gt; 289 aaaaaattgc agtgctgaag acactggacc cgcaaaagg ttctgggctc actgagttca cctgcgagtc agccctacc aaacaggctg ctggcattga ggtctgctac aaaaanart  agg ggc aag gtg aaa act gct cct att ccc at Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Il</pre>	t gcactgctct ggtctagtac 120 a atg gtc cca tgg ccc 175 Met Val Pro Trp Pro -55 c tct agg ttt cct ttc 223 e Ser Arg Phe Pro Phe -40 t tgg tct cca gca tct 271 s Trp Ser Pro Ala Ser 5 -20 c act ttg gcc ctg ctg 319 u Thr Leu Ala Leu Leu -5 a aaa ctt gca ggg caa 367 s Lys Leu Ala Gly Gln 10

Lys Ala Lys Lys Leu Pro Ser Phe Ser Ser Leu Pro Leu Thr Leu Trp  15 20 25  cca tta act cct caa ttt gct gag ctc act aca gtg gca caa aaa aaa 4	
and the net see can tit set see cir act aca did dea ead add add	.63
Pro Leu Thr Pro Gln Phe Ala Glu Leu Thr Thr Val Ala Gln Lys Lys	.03
30 35 40 45	
ttg agg tgg tcc ggg acc cta ggt tgg ggt cca gtt ccc agc tgg gtt	11
Leu Arg Trp Ser Gly Thr Leu Gly Trp Gly Pro Val Pro Ser Trp Val	
50 55 60	66
caa ttt ttt tta ggg tgaatggagg garagttggg gactgaaaas ccttcaaara  Gln Phe Phe Leu Gly	
65	526
Caatottatt acadtakttt ttottattt aaaktttet tetteetjaat	86
ktogtogete atgeetgtaa taateeeagg aetttgtgar accaaktttg aaggateaet	746
tgaacccagg aktttgarac cascctgggc aacatrgtra gacctcatct ctacaaaaaa	306
aaaaa	311
<210> 290	
<211> 625	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 210332	
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 210299</pre>	
<223> Von Heijne matrix	
score 8.10000038146973	
seq ITCLLAFWVPASC/IQ	
<221> polyA_signal	
<222> 594599	
<221> polyA_site	
<222> 613625	
<400> 290 acaggicsmc ttaacatoto tigatitgag coactoccae tgicateago tittoacotgg	60
<400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa	120
<400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg	
<400> 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc	120 180
<pre>&lt;400&gt; 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233
<pre>&lt;400&gt; 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180
<pre>&lt;400&gt; 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233
<pre>&lt;400&gt; 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233
<pre>&lt;400&gt; 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281
<pre>&lt;400&gt; 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281 329
<pre>&lt;400&gt; 290 acaggtcsmc ttaacatctc ttgatttgag ccactcccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281
<pre>&lt;400&gt; 290 acaggtcsmc ttaacatctc ttgatttgag ccactccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281 329 382 442
<pre>&lt;400&gt; 290 acaggtcsmc ttaacatctc ttgatttgag ccactccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281 329 382 442 502
<pre>&lt;400&gt; 290 acaggtcsmc ttaacatctc ttgatttgag ccactccac tgtcatcagc tttcacctgg attatcgtga cagcctccta ctgcttctct atcatgtggc cagagctatc ttccctaaaa atgcattgca tagttgatca agtcactctc tggcctaaaa ccttccttgg ctccctgctg ccctcaggat aaagtctgga cccctcagc atg gct tgt gag act cat ggt gtc</pre>	120 180 233 281 329 382 442

```
<210> 291
 <211> 684
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> CDS
 <222> 212..361
<221> sig_peptide
 <222> 212..319
 <223> Von Heijne matrix
      score 4.09999990463257
      seq HWLFLASLSGIKT/YQ
<221> polyA_signal
<222> 650..655
<221> polyA_site
<222> 673..684
<400> 291
atccccawns cactetetea cagagactgt tetttteett etgagaceet actccagett
                                                                        60
gtagttctaa atctgtgatt atgcactgtc tgtcttcctc ttgaggtcag gggccatttc
                                                                       120
ttttgttctc tgctatgctc aggacccaga tcaaaggagc tcagtaacta tttacaggcg
                                                                       180
tacatcatat gtggaggaca cttatgctgt g atg gcc cca cac aca gct tcc
                                                                       232
                                    Met Ala Pro His Thr Ala Ser
                                        -35
ttt ggg gtc tgt ccc ctg ctc tcc gtt acc cgc gtg gta gcc act gag
                                                                       280
Phe Gly Val Cys. Pro Leu Leu Ser Val Thr Arg Val Val Ala Thr Glu
                -25
                                     -20
cac tgg ctc ttc ctg gct tca ctc tct ggc atc aaa act tat cag tcc
                                                                      328
His Trp Leu Phe Leu Ala Ser Leu Ser Gly Ile Lys Thr Tyr Gln Ser
            -10
                                 -5
tac atc tca gtc ttt tgc aag gtg aca ctt atc tgattaccta attcacacra
                                                                      381
Tyr Ile Ser Val Phe Cys Lys Val Thr Leu Ile
                        10
aggtgttaat ggtggtaatg gcataktatt tattacccca ggggacccak aacggtggta
                                                                      441
tcaaaacata tcattcccca gtggtttaaa actctggtag ctttccargg aatccaaagt
                                                                      501
ggaatccagt ctccttagct gawttcacag ggccccgtct gcacaacttg gcttctgtcg
                                                                      561
getteectan ecetgaette ceaageetta gteateacee teteteecae ecagggetea
                                                                      621
gcacagtacc tggaacagtc aagccctcaa taaatgttta ctgagtgcat yaaaaaaaa
                                                                      681
aaa
                                                                      684
```

<211> 628

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 75..482

<221> sig\_peptide

<222> 75..128

<223> Von Heijne matrix
score 3.59999990463257
seq KMLISVAMLGAXA/GV

```
<221> polyA signal
<222> 595..600
<221> polyA site
<222> 618..627
<400> 292
aagtgagacc gegeggeaac agettgegge tgeggggage teeegtggge geteegetgg
                                                                  60
                                                                  110
ctgtgcaggc ggcc atg gat tcc ttg cgg aaa atg ctg atc tca gtc gca
            Met Asp Ser Leu Arg Lys Met Leu Ile Ser Val Ala
                                              -10
                           -15
                                                                  158
atg ctg ggc gca rgg gct ggc gtg ggc tac gcg ctc ctc gtt atc gtg
Met Leu Gly Ala Xaa Ala Gly Val Gly Tyr Ala Leu Leu Val Ile Val
                       1
acc ccg gga gag cgg cgg aag cag gaa atg cta aag gag atg cca ctg
                                                                  206
Thr Pro Gly Glu Arg Arg Lys Gln Glu Met Leu Lys Glu Met Pro Leu
                                  20
                                                                  254
Gln Asp Pro Arg Ser Arg Glu Glu Ala Ala Arg Thr Gln Gln Leu Leu.
           30
                              35
ctg gcc act ctg cag gag gca gcg acc acg cag gag aac gtg gcc tgg
                                                                  302
Leu Ala Thr Leu Gln Glu Ala Ala Thr Thr Gln Glu Asn Val Ala Trp
                           50
                                                                  350
agg aag aac tgg atg gtt ggc ggc gaa ggc gcc acg gga kgt cac
Arg Lys Asn Trp Met Val Gly Gly Gly Gly Ala Thr Gly Xaa His
                       65
                                          70
cgt gag acc gga ctt gcc tcc gtg ggc gcc gga cct tgg ctt ggg cgc
                                                                  398
Arg Glu Thr Gly Leu Ala Ser Val Gly Ala Gly Pro Trp Leu Gly Arg
                                      85 .
agg aat ccg agg cag ctt tct cct tcg tgg gcc can cgg aaa atc cgg
Arg Asn Pro Arg Gln Leu Ser Pro Ser Trp Ala Xaa Arg Lys Ile Arg
               95
                                  100
ame gaa aat wee atg cea gga etc tee ggg gte etg tgaactgeeg
                                                                  492
Xaa Glu Asn Xaa Met Pro Gly Leu Ser Gly Val Leu
           110
tegggtgage acgtgteece caaaccetgg actgactget traaggteeg caaggeggge
cagggccgag acgcgagtcg gatgtggtga actgaaagaa ccaataaaat catgttcctc
                                                                  612
                                                                  628
cammcaaaaa aaaaah
```

<211> 813

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 50..631

<221> sig\_peptide

<222> 50..244

<223> Von Heijne matrix seq LTLIGCLVTGVES/KI

<221> polyA signal

<222> 777..782

<221> polyA site

<222> 801..812

<400> 293 4	
aaggaaagga ttactcgagc cttgttagaa tcagacatgg cttcagggg atg cag gac Met Gln Asp -65	58
gct ccc ctg agc tgc ctg tca ccg act aag tgg agc agt gtt tct tcc Ala Pro Leu Ser Cys Leu Ser Pro Thr Lys Trp Ser Ser Val Ser Ser -60 -55 -50	106
gca gac tca act gag aag tca gcc tct gcg gca ggc acc agg aat ctg Ala Asp Ser Thr Glu Lys Ser Ala Ser Ala Ala Gly Thr Arg Asn Leu -45 -35	154
cct ttt cag ttc tgt ctc cgg cag gct ttg agg atg aag gct gcg ggc Pro Phe Gln Phe Cys Leu Arg Gln Ala Leu Arg Met Lys Ala Ala Gly -30 -25 -20 -15	202
att ctg acc ctc att ggc tgc ctg gtc aca ggc gtc gag tcc aaa atc Ile Leu Thr Leu Ile Gly Cys Leu Val Thr Gly Val Glu Ser Lys Ile -10 -5 1	250
tac act cgt tgc aaa ctg gca aaa ata ttc tcg agg gct ggc ctg gac Tyr Thr Arg Cys Lys Leu Ala Lys Ile Phe Ser Arg Ala Gly Leu Asp 5 10 15	298
aat cyg agg ggc ttc agc ctt gga aac tgg atc tgc atg gcg tat tat Asn Xaa Arg Gly Phe Ser Leu Gly Asn Trp Ile Cys Met Ala Tyr Tyr 20 25 30	346
gag agc ggc tac aac acc aca gcc car acg gtc ctg gat gac ggc agc Glu Ser Gly Tyr Asn Thr Thr Ala Gln Thr Val Leu Asp Asp Gly Ser 35 40 45 50	394
atc gac tay ggc atc ttc caa atc aac agc ttc gcg tgg tgc aga cgc  Ile Asp Tyr Gly Ile Phe Gln Ile Asn Ser Phe Ala Trp Cys Arg Arg  55 60 65	442
gga aag ctg aag gag aac aac cac tgc cay gtc gcc tgc tca gcc ttg Gly Lys Leu Lys Glu Asn Asn His Cys His Val Ala Cys Ser Ala Leu 70 75 80	490
rtc act gat gac ctc aca gat gca att atc tgt gcc arg aaa att gtt Xaa Thr Asp Asp Leu Thr Asp Ala Ile Ile Cys Ala Xaa Lys Ile Val 85 90 95	538
aaa gag aca caa gga atg aac tat tgg caa ggc tgg aag aaa cay tgt Lys Glu Thr Gln Gly Met Asn Tyr Trp Gln Gly Trp Lys Lys His Cys 100 105 110	586
gag ggg aga gac ctg tcc gas tgg aaa aaa ggc tgt gag gtt tcc Glu Gly Arg Asp Leu Ser Xaa Trp Lys Lys Gly Cys Glu Val Ser 115 120 125	631
taaactggaa ctggacccag gatgctttgc ascaacgccc tagggtttgc agtgaatgtc caaatgcctg tgtcatcttg tcccgtttcc tcccaatatt ccttctcaaa cttggagagg gaaaattaag ctatactttt aagaaaataa atatttccat ttaaatgtca amaaaaaaaa ah	691 751 811 813

<211> 778

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 154..576

<221> sig\_peptide

<222> 154..360

<223> Von Heijne matrix score 4.80000019073486 seq MMVLSLGIILASA/SF

<221> polyA signal <222> 737..742 <221> polyA site <222> 763..775 <400> 294 agtaaaaaa cactggaata aggaagggct gatgactttc agaagatgaa ggtaagtaga 60 aaccgttgat gggactgaga aaccagagtk aaaacctctt tggagcttct gaggactcag 120 ctggaaccaa cgggcacagt tggcaacacc atc atg aca tca caa cct gtt ccc 174 Met Thr Ser Gln Pro Val Pro aat gag acc atc ata gtg ctc cca tca aat gtc atc aac ttc tcc caa 222 . Asn Glu Thr Ile Ile Val Leu Pro Ser Asn Val Ile Asn Phe Ser Gln -55 270 ' gca gag aaa ccc gaa ccc acc aac cag ggg cag gat agc ctg aag aaa Ala Glu Lys Pro Glu Pro Thr Asn Gln Gly Gln Asp Ser Leu Lys Lys -45 -40 -35 cat cta cac gca gaa atc aaa gtt att ggg act atc cag atc ttg tgt 318 His Leu His Ala Glu Ile Lys Val Ile Gly Thr Ile Gln Ile Leu Cys -25 -20 ggc atg atg gta ttg agc ttg ggg atc att ttg gca tct gct tcc ttc 366 Gly Met Met Val Leu Ser Leu Gly Ile Ile Leu Ala Ser Ala Ser Phe -10 -5 tot cca aat ttt acc caa gtg act tct aca ctg ttg aac tct gct tac 414 Ser Pro Asn Phe Thr Gln Val Thr Ser Thr Leu Leu Asn Ser Ala Tyr 10 cca ttc ata gga ccc ttt ttt gtr akt aaa btt tct gag gag ggc agg 462 Pro Phe Ile Gly Pro Phe Phe Val Xaa Lys Xaa Ser Glu Glu Gly Arg 25 30 atg ggg caa ara ggg gag gaa rat vcc aat agc tta aac ttc cca sct 510 Met Gly Gln Xaa Gly Glu Glu Xaa Xaa Asn Ser Leu Asn Phe Pro Xaa 40 gcc agc ttg cta tkt ttg atc tgc cag gav caa gga ttc aac ggt gaa 558 Ala Ser Leu Leu Xaa Leu Ile Cys Gln Xaa Gln Gly Phe Asn Gly Glu 60 tct tgt tct cct gtc ggg targataaca ggggttgctt rattttagat 606 Ser Cys Ser Pro Val Gly 70 caatttctta tcagactcaa ataaacattt cttttgaaaa tcatcttatt cttcacatta 666 tcatcttgag ctatgatgga aactagtgas ktctctccag gtttaggcga aaaaaaaatc 726

catgaattag gataaagttg ggaaggaaca ttttatacaa aaaaaaaaah cc

778

<210> 295

<211> 1060

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 154..897

<221> sig\_peptide

<222> 154..360

<223> Von Heijne matrix
 score 4.80000019073486
 seq MMVLSLGIILASA/SF

<221> polyA\_signal <222> 1017..1022

<221> polyA\_site <222> 1044..1054

			•								1		,			
<40	)> 29	95										,				
															agtaga	60
															actcag	120
ctg	gaaco	caa	gggg	caca	gt to	gcaa	acaco	ato	_	-					ccc	174
									Met	Th	r Sei	c Gl			l Pro	
			· ;										-6			
			atc													222
Asn	Glu		Ţlе	Ile	Val	Leu		Ser	Asn	Val	Ile		Phe	Ser	GIn	
' '		-60					-55					-50				
			CCC													270
ATA		ьуs	Pro	GIU	Pro		Asn	GIN	GIY	GIN	_	ser	Leu	ьys	гуѕ	
	-45					-40					-35					270
			gca Ala													318
-30	neu	пть	Ald	GIU	-25	пув	val	116	GTÅ	-20	116	GIII	116	пец	-15	•
	3 t G	2+~	gta	++~		++~	~~~	2+0	a++		~~~	+a+	aat	+ ~ ~		366
			Val													300
Gry	Mec	MEC	vai	-10	261	neu	Gry	116	-5	neu	Ата	261	Ата	1	FIIC	
tct	cca	22 <b>+</b>	ttt		<b>C</b> 22	ata	act	tet	-	cta	tta	220	tot	_	tac	414
			Phe													273
DCI	FIO	5	FIIC	1111	GIII	vaı	10		1111	пси	пец	15	261	ATO	171	
cca	ttc	_	gga	CCC	` <del>+++</del>	+++		atc	atc	tct	aac		cta	tca	atc	462
			Gly													102
	20					25		110			30	JCI		501		
acc		aaa	aaa	agg	tta		aac	ctt	tta	ata		acc	acc	cta	att	510
			Lys													510
35		_,_	-,0	5	40					45					50	
	agc	att	ctg	agt		cta	tet	acc	cta		aat	ttc	att	avc		558
			Leu													
2				55					60		<b></b> 1			65		
tct	atc	aaa	cag		acc	tta	aat	cct		tca	cta	cak	tat	gag	ttq	606
			Gln													
		•	70					75					80			
gmc	aaa	aat	aat	ata	cca	aca	ara	akt	tat	gtt	yct	tac	ttt	tat	cat	654
Xaa	Lys	Asn	Asn	Ile	Pro	Thr	Xaa	Xaa	Tyr	Val	Xaa	Tyr	Phe	Tyr	His	
		85					90					95				
gat	tca	ctt	tat	acc	acg	gac	kgc	tat	aca	gcc	aaa	gcc	akt	ctg	gct	702
Asp	Ser	Leu	Tyr	Thr	Thr	Asp	Xaa	Tyr	Thr	Ala	Lys	Ala	Xaa	Leu	Ala	
	100					105					110					
			tct													750
	Thr	Leu	Ser	Leu		Leu	Ile	Cys	Thr		Leu	Glu	Phe	Cys		
115					120					125		•			130	
			act													798
Xaa	Val	Leu	Thr		Val	Leu	Arg	Trp	-	Gln	Ala	Tyr	Ser			
_				135					140					145		
			gta													846
Pro	GIY	Ser	Val	Leu	Phe	Leu	Pro		Ser	Tyr	He	GIY		ser	GIY	
			150					155					160			004
			aaa													894
met	ser		Lys	Met	Thr	His	_	Cys	GIÀ	Tyr	Glu		⊾eu	ren	Thr	
+	<b>L</b>	165					170	~~~				175				047
		gaaa	aaa	ggga	gaaa	ta ti	taat	caga	a ag	ttga	ttct	tat	gata	ata		947
Ser							~~~		<b>.</b>						<b></b> .	1000
															tttaaa	1007
gta	atga	aca	ttaa	aaaa	aa C	catta	<b>4000</b>	c ac	cgtc	aaaa	aaaa	aaaaı	mcc :	IIKT		1060

```
<210> 296
<211> 444
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 146..292
<221> sig_peptide
<222> 146..253
<223> Von Heijne matrix
     score 5.5
     seq FTSMCILFHCLLS/FQ
<221> polyA_signal
<222> 395..400
<221> polyA_site
<222> 433..444
<400> 296
aacttgggac aagaratcaa actttaaaga tggtctaaag cccctcttaa aggtctgact
                                                                   60
gtgtcggacc tctagagcta atctcactag atgtgagcca ttgtttatat tctagccatc
                                                                  120
ctttcatttc attctagaag acccc atg caa gtt ccc cac cta agg gtc tgg
                                                                  172
                          Met Gln Val Pro His Leu Arg Val Trp
                                                  -30
                              -35
                                                                  220
aca cag gtg awa gat acc ttc att ggt tat aga aat ttg gga ttt aca
Thr Gln Val Xaa Asp Thr Phe Ile Gly Tyr Arg Asn Leu Gly Phe Thr
                           -20
                                                                  268
agt atg tgc ata ttg ttc cac tgt ctt ctt agc ttt cag gtt ttc aaa
Ser Met Cys Ile Leu Phe His Cys Leu Leu Ser Phe Gln Val Phe Lys
                       -5
                                          1
    -10
aag aaa aga aaa ctt ara ctt ttc tgatgttctt ttttacgtaa ataaccattt
                                                                  322
Lys Lys Arg Lys Leu Xaa Leu Phe
               10
tattgttgtt ttgctttttc tgccttcaaa ctactcccac aggccaaata tavctggctg
                                                                  382
442
                                                                  444
<210> 297
<211> 754
<212> DNA
<213> Homo sapiens
```

<220>

<221> CDS

<222> 126..383

<221> sig\_peptide

<222> 126..167

<223> Von Heijne matrix score 7.5 seq VALNLILVPCCAA/WC

<221> polyA\_signal

<222> 726..731

<221> polyA\_site

<222> 743..754

•••	
<400> 297	
aattgtatgt tacgatgttg tattgatttt taagaaagta attkr	atttg taaaacttct 60
gctcgtttac actgcacatt gaatacaggt aactaattgg wwgga	gaggg gaggtcactc 120
ttttg atg gtg gcc ctg aac ctc att ctg gtt ccc tgc Met Val Ala Leu Asn Leu Ile Leu Val Pro Cys -10 -5	
tgt gac cca cgg agg atc cac tcc cag gat gac gtg c	tc cgt agc tct 218
Cys Asp Pro Arg Arg Ile His Ser Gln Asp Asp Val I 5 10	eu Arg Ser Ser 15
got got gat act ggg tot gog atg dag ogg ogt gag g	cc tgg gct ggt 266
Ala Ala Asp Thr Gly Ser Ala Met Gln Arg Arg Glu A 20 25 3	la Trp Ala Gly
tgg aga agg tca caa ccc ttc tct gtt ggt ctg cct t	ct gct gaa aga 314
Trp Arg Arg Ser Gln Pro Phe Ser Val Gly Leu Pro S 35 40 45	er Ala Glu Arg
ctc gag aac caa cca ggg aag ctg tcc tgg agg tcc c	tg gtc gga gag 362
Leu Glu Asn Gln Pro Gly Lys Leu Ser Trp Arg Ser I	eu Val Gly Glu
50 55 60	65
gga cat aga atc tgt gac ctc tgacrrctgt gaasccacco	tgggctacar 413
Gly His Arg Ile Cys Asp Leu 70	
aaaccacagt cttcccagca attattacaa ttcttgaatt ccttg	
cctttcaaag cacttaaktg tkrratctaa cgtkttccag tgtct	
aaaaatcaga acaaaactto tattatocag agtcatggga gagta	
taatgttttg ggaaacactg aaatgaaatc ttcccagtat tataa	= =
aaaagaaact tttctgaatg cctacctggc ggtgtatacc aggca	
aagatgaaaa agaataaaaa cttttgagga aaaaaaaaaa	754

<211> 629

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 66..497

<221> sig\_peptide

<222> 66..239

<223> Von Heijne matrix score 5.40000009536743 seq QLLDSVLWLGALG/LT

<221> polyA\_signal

<222> 594..599

<221> polyA\_site

<222> 618..629

<400> 298

aactcccaga atgctgacca aagtgggagg agcactaggt cttcccgtca cctccacctc	60
totoc atg acc egg ctc tgc tta ccc aga ccc gaa gca egt gag gat eeg Met Thr Arg Leu Cys Leu Pro Arg Pro Glu Ala Arg Glu Asp Pro	110
-55 -50 -45	
atc cca gtt cct cca agg ggc ctg ggt gct ggg gag ggg tca ggt agt	158
Ile Pro Val Pro Pro Arg Gly Leu Gly Ala Gly Glu Gly Ser Gly Ser	
-40 -35 -30	
cca gtg cgt cca cct gta tcc acc tgg ggc cct agc tgg gcc cag ctc	206
Pro Val Arg Pro Pro Val Ser Thr Trp Gly Pro Ser Trp Ala Gln Leu	

		25					2.0					-15				
cta	gac	-25	atc	cta	tgg	cta	-20 aga	gca	cta	gga	cta	-15 aca	atc	caq	qca	254
					Trp											
	-10					-5					1				5	202
gtc	Dhe	tcc	acc	act	ggc Gly	cca	gcc	ctg	ctg	ctg	Ctt	ctg	grc Val	agc	Phe	302
vaı	PHE	SEL	1111	10	СТУ	PIO	Ala	Бец	15	ьеu	пец	Dea	Val	20	1110	
					ctc											350
Leu	Thr	Phe	_	Leu	Leu	His	Arg		Ala	Val	Thr	Leu		His	Ser	
aca	220	ttc	25 tca	cca	999	מככ	aga	30 atc	agg	aaa	cca	ata	35 aag	atc	cta	398
					Gly											•••
		40	•				45					50				
					tac											446
Asp	Ser 55	Arg	Arg	Leu	Tyr	Ser 60	Cys	гуѕ	Trp	vaı	65	ser	GIN	Asp	ASII	
tta		tcc	agg	aaq	cac		tạc	tqc	tqc	tca		ggc	tgg	gcc	cgc	494
					His											
70					75					80					85	
tee tyanantees tyseless to small the same to the same type type type type type type type typ													547			
Ser ccatccttgg gcctgakanc ccctccccac aactcagtgt ccttcaaata tacaatgacc													atgacc	607		
				-	aa aa				•	, ,					•	629
<210	)> 2!	99														
<21	1> 70	55														
	2 > DI		_													
<21:	3 > H	omo s	sapi	ens												
<220	) >															
<22	1> CI	os														
<22	2 > 4	94	11													
-22	1 - 0:	ia n	eptio	40												
		99	-	ae.												
				e mai	trix									•		•
					00383		7									
	S	ed L	VLTL	CTLP	LAVA,	/SA										
<22	1 > n	avio	sig	nal												
	_	32														
	_		sit	e												
<22.	2> /.	50	/63													
<40	0 > 2	99														
aaa	gatc	cct	gcag	cccg	gc ag	ggag	agaa	g gc	tgag	cctt	ctg	gcgt			g agg	57
													Me	t Gl <sup>.</sup> -1	u Arg	
ctc	atc	cta	acc	cta	tgc	acc	ctc	cca	cta	act	ata	aca	tct	_	_	105
					Cys											
			-10		-			-5					1			
					gct											153
Cys	Ala 5	Thr	Thr	Pro	Ala	Arg	Asn	Leu	Ser	Cys	Tyr 15	Gln	Cys	Phe	гÀг	
atc	_	aac	taa	aco	gag		cca	ccc	acc	taa		agc	cca	cta	gac	201
					Glu											
20			_		25					30	_				35	
caa	gtc	tgc	atc	tcc	aac	gag	gtg	gtc	gtc	tct	ttt	agt	gag	tcy	CCC	249
GID	νal	cys	тте	ser	ASD	uيى	AGT	val	val	ser	rne	ser	GIU	Ser	Pro	

WO 99/31236 -218- PCT/IB98/02122 -

40 45 50											
ccg ggc aga ggg cas gtg cca bgt gcc ggg gaa kgg ccg gtg ccc ccg	297										
Pro Gly Arg Gly Xaa Val Pro Xaa Ala Gly Glu Xaa Pro Val Pro Pro	•										
55 60 65											
cct ctc wkc gac tta bct atg act cct cgg ckc ycc agg gcc tgg ggc	345										
Pro Leu Xaa Asp Leu Xaa Met Thr Pro Arg Xaa Xaa Arg Ala Trp Gly											
70 75 80											
cck gtg ggt ccd aaa gtg cct cct gct gtc tct ccc gcg ctg ggc tcg	393										
Pro Val Gly Pro Lys Val Pro Pro Ala Val Ser Pro Ala Leu Gly Ser	•										
85 90 95											
ggc gag cat ccs rva btg tgaatkkkga cttttttctc ckccatttga	441										
Gly Glu His Pro Xaa Xaa											
100 105											
agtgtcacta ggaactgtca gcaggacaaa ggctctgatg tcactgaatt tacaaaraca	501										
gcaggaacrs ackggtgggg atgggcagct gttcrargcr atgggtkatc tgcccttcct	561										
ggcacagcac artacacctg ccatacaacc carcatcagg cakgctgcac tggaatcgat	621										
acagtgtatg acaatgtcat atagtataac acaacataat gaatataacg tgtatattgc											
aacttaatat aatacgatgt aatataatgc tacataatac aacataatat aataaaatag	. 741										
aatgcaacac aaaaaaaaa aacc	765										
<210> 300											
<211> 623											
<212> DNA											
<213> Homo sapiens											
•••											
<220>											
<221> CDS											
<222> 49534											
<221> sig_peptide											
<222> 4996											
<223> Von Heijne matrix											
score 10.1000003814697											
seq LVLTLCTLPLAVA/SA											
alle malua aigmal											
<221> polyA_signal	•										
<222> 593598											
<222> 593598											
<221> polyA_site											
<221> polyA_site <222> 612623											
<221> polyA_site <222> 612623 <400> 300	53										
<221> polyA_site <222> 612623  <400> 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg	57										
<221> polyA_site <222> 612623  <400> 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg Met Glu Arg	57										
<221> polyA_site <222> 612623  <400> 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg Met Glu Arg -15											
<221> polyA_site <222> 612623  <400> 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg	57 105										
<221> polyA_site <222> 612623  <400> 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg											
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>	105										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>											
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagateeet geageeegge aggagagaag getgageett etggegte atg gag agg</pre>	105										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>	105										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>	105										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>	105										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>	105 153 201										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>	105										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>	105 153 201										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>	105 153 201 249										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatcctt gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>	105 153 201										
<pre>&lt;221&gt; polyA_site &lt;222&gt; 612623  &lt;400&gt; 300 aaagatccct gcagcccggc aggagagaag gctgagcctt ctggcgtc atg gag agg</pre>	105 153 201 249										

atg Met	aak Xaa	Phe	gaa Glu	tgg Trp	tcg Ser	Pro	Ala	ccc Pro	atg Met	gtg Val	caa Gln	GIÀ	gtg Val	atc Ile	acc Thr	345
		70					75					80	200	cc2	cac	393
agg Arg	Arg	tgc Cys	tgt Cys	tcc Ser	tgg Trp	Ala	ctc Leu	tgc Cys	aac Asn	agg Arg	gca Ala 95	Leu	acc Thr	Pro	Gln	373
	85					90		~~~	ata	cta		cad	gac	cct	tca	441
gag	999	cgc	tgg	gcc	ctg	CIA	999	999	T.em	Len	Len	Gln	gac Asp	Pro	Ser	
	GIY	Arg	Trp	Ala		Лаа	GIY	Gry	пец	110	DCu	· · · ·		•	115	
100					105	ata		cca	cad		aaa	ctc	cca	ctc	tac	489
agg	ggc	ara	aaa	acc	rgg	919	250	Dro	Gln	Len	SPS	Leu	Pro	Leu	Cvs	
Arg	GIY	хаа	гÀг	120	пр	vaı	Arg	, FIO	1.25	1100	Q-J			130	•	
			+		000	ctc	Fac	cca		gaa	acc	caq	gaa	qqa		534
CLL	Dwo	awt	60~	Acr	Dro	Len	Cvs	Pro	Xaa	Glu	Thr	Gln	Glu	Gly		
ьeu	PIO	naa	135	ASII		LCu	0,70	140					145	•		
+	cacto	744	TO D		ra c	rtato	rcati		gacc	acra	ctt	cacco	ctc t	tgga	aracaa	594
taa	actci	ara :	39°9'	CCCA	aa a:	22222	aaaa	- 55.	J				·	_		623
taa	actu	cca	ęgcc.	ccca	2a u	auuuc										
	0 > 3	Λ1							•	•						
																•
	1 > 5											•				
	2 > D			000											•	
<21	3> H	Omo	sapı	ens												
	٥.															
<22		<b>D</b> 0														
	1> C									•						
<22	2> 8	64	15													
		,	}	ا ـ												
	1> S			ae												
	2 > 8		•													
<22	:3> V						_									
						7348	0									
	s	eq F	TIGL	TLLL	GXQA	/MP										
				,												
	21> p			maı												
<22	22 > 5	40	545													
	21> p			:e												
<22	22 > 5	60	571													
<40	00 > 3	301									. + ~ 1		272	ccaa	aaggaa	60
aaa	aaact	cac	ccas	gtgag	jtg t	gago	acti	a au	jaay	.a.c.	- ct	ctt	.agu · att	tto	aaggaa acc	112
aga	aagaa	aaaa	pggg	caaa	ag o	caaa	ate	arc	To	y act	9 90	Lo	, Wal	Dhe	acc Thr	
									ı ne	ı Met	L va.	-15				
							-20							aat	cac	160
at	t ggg	g cta	a act	ttg	cts	g cta	gga	a rti	. caa	a gc	o Mo	9 000	. Mls	Δer	cgc	
Il			ı Thi	r Lei	ı Lei		r GT	ухаа	3 671	1 Ale	a Me	L PIC	) Ale	, Wor	Arg 5	
	-10	כ				-5					1					208
ct	c tct	t tg	c ta	c aga	a aag	gata	t cta	a aaa	a gar	c ca	c aa	c ty	. cac	. 201	ctt	200
Le	u Sei	r Cy	з Ту:	r Ar	g Ly:	s Ile	e Le	u Ly:		о на	s As:	n Cys	5 HIE	20 191	ı Leu	
				10					15					20		256
CC	g gaa	a gg	a gt	a gci	t ga	c ct	gac	a ca	g at	t ga	t gt	c aai	t gto	cas	g gat	250
Pr	o Gli	u Gl	y Va	l Ala	a As	p Let	ı Th	r Gl	n Il	e As	p Va	l As	n Val	L GII	n Asp	
			25					30					35			204
ca	t tt	c tg	g ga	t gg	g aa	g gga	a tg	t ga	g at	g at	c tg	t ta	c tgo	c aac	ttc	304
Hi	s Ph	e Tr	p As	p Gl	у Ьу	s Gly	у Су	s Gl	u Me	t Il	e Cy	s Ty	r Cys	s Ası	n Phe	
		40					45					50				
aa	g ca	a at	t gc	t ct	g ct	g cc	c aa	a ag	a cg	t tt	t ct	t tg	g ac	c aa	a gat	352
Lν	s Ar	g Il	e Āl	a Le	u Le	u Pro	o Ly	s Ar	g Ar	g Ph	e Le	u Tr	p Th:	r Ly	s Asp	
	55					60					65					
ct	c tt	t ca	t qa	t tc	c tt	g ca	a ca	a tc	a at	g ag	a at	c tt	c at	g ta	t tct	400
			J			_				_						

Leu Phe Arg Asp Ser Leu Gln Gln Ser Met Arg Ile Phe Met Tyr Ser	
ggc gaa cac cat tcc tgatttccca caaactgcac tacatcagta taactgcatt Gly Glu His His Ser	455
90 tctagtttct atatagtgca atagagcata gattctataa attcttactt gtctaagaaa gtaaatctgt gttaaacaag tagtaataaa agttaattca atccaaaaaa aaaaaa	515 571
<210> 302 <211> 612 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 56268	
<221> sig_peptide <222> 56100 <223> Von Heijne matrix score 4.59999990463257 seq LLTHNLLSSHVRG/VG	
<221> polyA_signal <222> 584589	
<221> polyA_site <222> 601612	
<400> 302 ctaatcgaaa agggggattt tccggttccg gcctggcgag agtttgtgcg gcgac atg Met -15	58
aaa ctg ctt acc cac aat ctg ctg agc tcg cat gtg cgg ggg gtg ggg Lys Leu Leu Thr His Asn Leu Leu Ser Ser His Val Arg Gly Val Gly	106
tcc cgt ggc ttc ccc ctg cgc ctc cag gcc acc gag gtc cgt atc tgc Ser Arg Gly Phe Pro Leu Arg Leu Gln Ala Thr Glu Val Arg Ile Cys 5 10 15	154
cct gtg gaa ttc aac ccc aac ttc gtg gcg cgt atg ata cct aaa gtg Pro Val Glu Phe Asn Pro Asn Phe Val Ala Arg Met Ile Pro Lys Val 20 25 30	202
gag tgg tcg gcg ttc ctg gag gcg rmc gat aac ttg cgt ctg atc cag Glu Trp Ser Ala Phe Leu Glu Ala Xaa Asp Asn Leu Arg Leu Ile Gln 35 40 45 50	250
gtg ccg aga agg gcc ggt tgagggatat gaggagaatg aggagtttct Val Pro Arg Arg Ala Gly	298
gaggaccatg caccacctgc tgctggaggt ggamstgaka gagggcaccc tgcagtgccc ggaatctgga cgtatgttcc ccatcagccg cgggatcccc aacatgctgc tgagtgaaga ggaaactgag agttgattgt gccaggcgcc agtttttctt gttatgactg tgtatttttg ttgatctata ccctgtttcc gaattctgcc gtgtgtatcc ccaacccttg acccaatgac accaaacaca gtgtttttga gctcggtatt atatattttt ttctcattaa aggtttaaaa ccaaaaaaaa aaaa	358 418 478 538 598 612

<211> 539

<212> DNA

```
<213> Homo sapiens
<220>
<221> CDS
<222> 32..328
<221> sig_peptide
<222> 32..103
<223> Von Heijne matrix
      score 4.59999990463257
      seg FFIFCSLNTLLLG/GV
<221> polyA_signal
<222> 508..513
<221> polyA site
<222> 528..539
<400> 303
aacaactatc ctgcctgctg cttgctgcac c atg aag tct gcc aag ctg gga
                                                                       52
                                   Met Lys Ser Ala Lys Leu Gly
                                                    -20
ttt ctt cta aga ttc ttc atc ttc tgc tca ttg aat acc ctg tta ttg
                                                                      100
Phe Leu Leu Arg Phe Phe Ile Phe Cys Ser Leu Asn Thr Leu Leu Leu
                                                 -5
                            -10
                                                                      148
ggt ggt gtt aat aaa att gcg gag aag ata tgt gga gac ctc aaa gat
Gly Gly Val Asn Lys Ile Ala Glu Lys Ile Cys Gly Asp Leu Lys Asp
                    5
                                                                      196
ccc tgc aaa ttg gac atg aat ttt gga agc tgc tat gaa gtt cac ttt
Pro Cys Lys Leu Asp Met Asn Phe Gly Ser Cys Tyr Glu Val His Phe
                                    25
                20
aga tat ttc tac aac aga acc tcc aaa aga tgt gaa act ttt gtc ttc
                                                                      244
Arg Tyr Phe Tyr Asn Arg Thr Ser Lys Arg Cys Glu Thr Phe Val Phe
                                40.
tcc agc tgt aat ggc aac ctt aac aac ttc aag ctt aaa ata gaa cgt
                                                                      292
Ser Ser Cys Asn Gly Asn Leu Asn Asn Phe Lys Leu Lys Ile Glu Arg
                            55
        50
                                                                      338
gaa gta kcc tgt gtt gca aaa tac aaa cca ccg agg tgagaggatg
Glu Val Xaa Cys Val Ala Lys Tyr Lys Pro Pro Arg
                         70
tgaactcatg aagttgtctg ctgcaccatc cgaaataaag acacaagaaa attcaractg
                                                                      398
                                                                      458
atttwgaaat ctttgttwta tttccmymak ggcgwktaag cttccatatg tttgctattt
                                                                      518
tectgacect agttttgtet tteetggaaa ttaactgtat gakeattasa atgaaagagt
                                                                       539
ctttctgtca aaaaaaaaa a
```

-221-

<210> 304 <211> 964 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 21..527 <221> sig\_peptide <222> 21..95

<223> Von Heijne matrix score 8.5 seq LKVLLLPLAPAAA/QD

<221> polyA signal <222> 921..926 <221> polyA site <222> 953..963 <400> 304 agggeggate tteteeggee atg agg aag eea gee get gge tte ett eee tea Met Arg Lys Pro Ala Ala Gly Phe Leu Pro Ser -20 ctc ctg aag gtg ctg ctc ctg cct ctg gca cct gcc gca gcc cag gat 101 Leu Leu Lys Val Leu Leu Pro Leu Ala Pro Ala Ala Ala Gln Asp -10 tog act cag god tod act coa ggd agd cot otd tot cot acc gaa tac Ser Thr Gln Ala Ser Thr Pro Gly Ser Pro Leu Ser Pro Thr Glu Tyr 10 15 caa cgc ttc ttc gca ctg ctg act cca acc tgg aag gca gar act acc 197 Gln Arg Phe Phe Ala Leu Leu Thr Pro Thr Trp Lys Ala Glu Thr Thr 25 30 tgc cgt ctc cgt gca acc cac ggc tgc cgg aat ccc aca ctc gtc cag 245 Cys Arg Leu Arg Ala Thr His Gly Cys Arg Asn Pro Thr Leu Val Gln 40 45, ctg gac caa tat gaa aac cac ggc tta gtg ccc gat ggt gct gtc tgc 293 Leu Asp Gln Tyr Glu Asn His Gly Leu Val Pro Asp Gly Ala Val Cys .55 60 tcc aac ctc cct tat gcc tcc tgg ttt gag tct ttc tgc cag ttc act 341 Ser Asn Leu Pro Tyr Ala Ser Trp Phe Glu Ser Phe Cys Gln Phe Thr 75 cac tac cgt tgc tcc aac cac gtc tac tat gcc aag aga gtc ctg tgt 389 His Tyr Arg Cys Ser Asn His Val Tyr Tyr Ala Lys Arg Val Leu Cys 90 tcc cag cca gtc tct att ctc tcw cct aac act ctc aag gag ata gaa 437 Ser Gln Pro Val Ser Ile Leu Ser Pro Asn Thr Leu Lys Glu Ile Glu 105 110 sct tca gct gaa gtc tca ccc acc aca gat gac ctc ccc cat ctc acc 485 Xaa Ser Ala Glu Val Ser Pro Thr Thr Asp Asp Leu Pro His Leu Thr 120 125 cca ctt cac agt gac aga acg cca gac ctt cca gcc ctg gcc 527 Pro Leu His Ser Asp Arg Thr Pro Asp Leu Pro Ala Leu Ala 135 140

tgagaggetc agcaacaacg tggaagaget cetacaatee teettgteee tgggaggeea

ggagcaagcg ccagagcaca agcaggagca aggagtggag cacaggcagg agccgacaca

agaacacaag caggaagagg ggcagaaaca ggaagagcaa gaagaggaac aggaagagga

gggaaagcag gaagaaggac aggggactaa ggagggacgg gaggctgtgt ctcagctgca gacagactca gagcccaagt ttcactctga atctctatct tctaaccctt cctctttgc

tccccgggta cganaagtag agtctactcc tatgataatg gagaacatcc aggagctcat

tcgatcagcc caggaaatag atgaaatgaa tgaaatatat gatgagaact cctactggag

587

647

707

827

887

947

964

<210> 305

<211> 684

<212> DNA

<213> Homo sapiens

aaaccaaaaa aaaaaak

<220>

<221> CDS

<222> 147..647

<221> sig\_peptide

<222> 147..374

<223> Von Heijne matrix score 3.5 seq LASASELPLGSRP/AP

<221> polyA\_site <222> 668..681

<400> 305 60 aactteetgt gageeeggeg gtgacaaegg caacatggee egtgaaegga getgaagteg acgacttctc ctrgrarmcc ccgactgagg cggagacgaa ggtgctgcag gcgcgacggg 120 173 ageggcaaga tegeatetee eggete atg gge gae tat etg etg ege ggt tae Met Gly Asp Tyr Leu Leu Arg Gly Tyr -75 cgc atg ctg ggc gag acg tgt gcg gac tgc ggg acg atc ctc ctc caa 221 Arg Met Leu Gly Glu Thr Cys Ala Asp Cys Gly Thr Ile Leu Leu Gln -60 gac aaa cag cgg aaa atc tac tgc gtg gct tgt cag gaa ctc gac tca 269 Asp Lys Gln Arg Lys Ile Tyr Cys Val Ala Cys Gln Glu Leu Asp Ser -45 gac gtg gat aaa gat aat ccc gct ctg aat gcc cag gct gcc ctc tcc 317 Asp Val Asp Lys Asp Asn Pro Ala Leu Asn Ala Gln Ala Ala Leu Ser -30 -25 caa gct cgg gag cac cag ctg gcc tca gcc tca gag ctc ccc ctg ggc 365 Gln Ala Arg Glu His Gln Leu Ala Ser Ala Ser Glu Leu Pro Leu Gly -10 -15 tct cga cct gcg ccc caa ccc cca gta cct cgt ccg gag cac tgt gag 413 Ser Arg Pro Ala Pro Gln Pro Pro Val Pro Arg Pro Glu His Cys Glu 461 gga gct gca gca gga ctc aag gca gcc cag ggg cca cct gct cct gct Gly Ala Ala Gly Leu Lys Ala Ala Gln Gly Pro Pro Ala Pro Ala 20 gtg cct cca aat aca rat gtc atg gcc tgc aca cag aca gcc ctc ttg 509 Val Pro Pro Asn Thr Xaa Val Met Ala Cys Thr Gln Thr Ala Leu Leu 557 caa aag ctg acc tgg gcc tct gct gaa ctg ggc tct anc acc tcc cyg Gln Lys Leu Thr Trp Ala Ser Ala Glu Leu Gly Ser Xaa Thr Ser Xaa 50 gga aaa mta gca tcc agc tgt gtg gcc tta tcc gcg cat gtg cgg agg 605 Gly Lys Xaa Ala Ser Ser Cys Val Ala Leu Ser Ala His Val Arg Arg 70 ccc tgc gca gcc tgc agc agc tac agc act aag aga agc ccc 647 Pro Cys Ala Ala Cys Ser Ser Tyr Ser Thr Lys Arg Ser Pro

85

tgagaaaaac ctctagaaaa acaaaaaaaa aaaaccc

684

<210> 306 <211> 693 <212> DNA <213> Homo sapiens

<220>

<221> CDS

<222> 262..471

<221> sig\_peptide <222> 262..306 <223> Von Heijne matrix score 3.5 seq LCFLLPHHRLQEA/RQ WO 99/31236 -224 - PCT/IB98/02122

<221> polyA_signal	
<222> 663668	
<221> polyA_site	
<222> 682693	
122 00203	
<400> 306	
atttcgcggc gctcgcbgma cyhsgwtgtt cagcaccttc ggtccggttg aggttgtcaa	60
gtcggmccaa acaggttgtt tctctgcagt ttccaacatg gcagggmsgt ttaatagaca	120
tggataagaa gtccactcac agaaatcctg aagatgccag ggctggcaaa tatgaaggta	180
aacacaaacg aaagaaaaga agaaagcaaa accaaaacca gcaccgatcc cgacatagat	240
cagtgacgtc tttttcttca g atg atc cta tgt ttc ctt ctt cct cat cat	291
Met Ile Leu Cys Phe Leu Leu Pro His His	
-15 -10	
cgt ctt cag gaa gcc aga cag att caa gta ttg aag atg ctt cca agg	339
Arg Leu Gln Glu Ala Arg Gln Ile Gln Val Leu Lys Met Leu Pro Arg	
-5 <u>1</u> 5 10	
gaa aaa tta aga aga aga gaa gag aga aaa caa ata aat ggg aaa aaa	387
Glu Lys Leu Arg Arg Arg Glu Glu Arg Lys Gln Ile Asn Gly Lys Lys	
15 20 25	
raa agg aca aaa tat gaa aca cca aga aaa rga raa gga aaa aaa gga	435
Xaa Arg Thr Lys Tyr Glu Thr Pro Arg Lys Xaa Xaa Gly Lys Lys Gly	
30 35 40	
gga aac mac cmc wtw tkt cmc ctt tcc aar agg gac tgaaactggg	481
Gly Asn Xaa Xaa Xaa Xaa Leu Ser Lys Arg Asp	401
. <u></u>	
	F 4 3
ctgacccttt tgatttccaa vctcascgtt ttggtgtaag gcggccaaar aaggatgcgg	541
	601
acatettea cactaagtte agacteatga aaccaatett cagatgetet gtaaaccaca	661
taataaagag tttggaaatt aaaaaaaaar aa	693
<210> 307	
<211> 1656	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 741216	
<221> sig_peptide	
<222> 74172	
<223> Von Heijne matrix	
score 5.80000019073486	
seq XLCLGMALCPRQA/TR	
<221> polyA_signal	
<222> 16271632	
<221> polyA_site	
<222> 16401652	
<400> 307	
atctcttggc gtctcaacgt tcggatcagc agcttttttc cattctctct ctccacttct	60
tcagtgagca gcc atg agt tgg act gtg cct gtt gtg cgg gcc agc cag	109
Met Ser Trp Thr Val Pro Val Arg Ala Ser Gln	-03
-30 -25	
aga gtg agc tcg gtg gga gcg aat ktc cta tgc ctg ggg atg gcc ctg	157
Arg Val Ser Ser Val Gly Ala Asn Xaa Leu Cys Leu Gly Met Ala Leu	157
-20 -15 -10	

tgt																
-					Thr				Leu					ctc Leu 10		205
-5					1				5							
			Ser					Val					Ile	gag Glu		253
			15					20					25			
ttc	act	tcc	gar	aag	CCC	gtt	cat	cac	agt	aag	gtc	tcc	atc	ata	gga	301
														Ile		
						~~~									~~~	240
														aaa Lys		349
++~		ant.	~~~	c++	~~~	ctt	ata	ant.	ctt	ant.		<b>720</b>	222	ctg	220	397
																, , , , , ,
60					65					70				Leu	75	,
ggt	gag	acr	atg	gat	ctt	caa	cat	ggc	agc	cct	ttc	acg	aaa	atg	cca	445
														Met 90		
+	-++	~++				~~+	+	+++					+00		at a	493
														aac		473
Asn	He	Val	Cys 95	Ser	Lys	Xaa	Tyr	Phe 100	Val	Thr	Ala	Asn	Ser 105	Asn	Leu	
ata	att	atc	aca	qca	aat	qca	cqc	caa	raa	aaq	qqa	gaa	acq	cgc	ctt	541
														Arg		
val	110		1111	ATA	Gry	AIA	-	GIII	Add	цуз	GLY		1111	,mg	БСС	
		110					115					120				
aat	tta	stc	cag	cga	aat	gtg	gcc	atc	ttc	aag	tta	atg	att	tcc	agt	589
										Lys				Ser		
2++		cad	tac	200	ccc		tac	222	cta			att	tee	aat	cca	637
																057
TTE	vaı	GID	Tyr	ser	Pro	His	Cys	гàг	Leu	тте	тте	Val.	Ser	Asn		
140				•	145					150					155	
ata	gat	atc	tta	act	tat	gta	act	taa	aaq	tta	agt	gca	ttt	ccc	aaa	685
														Pro		
220																
	cat	att	att	aga	agc	aac	tat	aat	cta	ata	mha	act	cat	ttt	cat	733
	_			Gly	_		_		_			_		ttt Phe		733
Asn	Arg	Ile	Ile 175	Gly	Ser	Gly	Cys	Asn 180	Leu	Ile	Xaa	Ala	Arg 185	Phe	Arg	
Asn ttc	Arg	<pre>Ile att</pre>	Ile 175 gga	Gly	Ser	Gly	Cys	Asn 180 atc	Leu	Ile tct	Xaa gaa	Ala	Arg 185 tgc	Phe	Arg gga	733 781
Asn ttc	Arg	<pre>Ile att</pre>	Ile 175 gga	Gly	Ser	Gly	Cys	Asn 180 atc	Leu	Ile tct	Xaa gaa	Ala	Arg 185 tgc	Phe	Arg gga	
Asn ttc	Arg	<pre>Ile att</pre>	Ile 175 gga	Gly	Ser	Gly	Cys	Asn 180 atc	Leu	Ile tct	Xaa gaa	Ala	Arg 185 tgc	Phe	Arg gga	
Asn ttc Phe	Arg ttg Leu	Ile att Ile 190	Ile 175 gga Gly	Gly caa Gln	Ser aag Lys	Gly ctt Leu	Cys ggt Gly 195	Asn 180 atc Ile	Leu cat His	Ile tct Ser	Xaa gaa Glu	Ala agc Ser 200	Arg 185 tgc Cys	Phe cat His	Arg gga Gly	781
Asn ttc Phe tgg	Arg ttg Leu atc	Ile att Ile 190 ctc	Ile 175 gga Gly gga	Gly caa Gln gag	Ser aag Lys cat	Gly ctt Leu gga	Cys ggt Gly 195 gac	Asn 180 atc Ile tca	Leu cat His	Ile tct ser gtt	Xaa gaa Glu cct	Ala agc Ser 200 gtg	Arg 185 tgc Cys	Phe cat His	Arg gga Gly gga	
Asn ttc Phe tgg Trp	Arg ttg Leu atc Ile 205	Ile att Ile 190 ctc Leu	Ile 175 gga Gly gga Gly	caa Gln gag Glu	Ser aag Lys cat His	Gly ctt Leu gga Gly 210	Cys ggt Gly 195 gac Asp	Asn 180 atc Ile tca Ser	Leu cat His agt Ser	Ile tct Ser gtt Val	Xaa gaa Glu cct Pro 215	agc Ser 200 gtg Val	Arg 185 tgc Cys tgg Trp	Phe cat His agt Ser	Arg gga Gly gga Gly	781 829
Asn ttc Phe tgg Trp	Arg ttg Leu atc Ile 205	Ile att Ile 190 ctc Leu	Ile 175 gga Gly gga Gly	caa Gln gag Glu	Ser aag Lys cat His	Gly ctt Leu gga Gly 210	Cys ggt Gly 195 gac Asp	Asn 180 atc Ile tca Ser	Leu cat His agt Ser	Ile tct Ser gtt Val	Xaa gaa Glu cct Pro 215	agc Ser 200 gtg Val	Arg 185 tgc Cys tgg Trp	Phe cat His	Arg gga Gly gga Gly	781
Asn ttc Phe tgg Trp	Arg ttg Leu atc Ile 205 aac	Ile att Ile 190 ctc Leu ata	Ile 175 gga Gly gga Gly gct	Gly caa Gln gag Glu	Ser aag Lys cat His	Ctt Leu gga Gly 210 cct	Cys ggt Gly 195 gac Asp	Asn 180 atc Ile tca ser	cat His agt Ser	tct ser gtt Val ctg	Xaa gaa Glu cct Pro 215 aac	Ala agc ser 200 gtg Val tct	Arg 185 tgc Cys tgg Trp	Phe cat His agt Ser ata	Arg gga Gly gga Gly gga	781 829
ttc Phe tgg Trp gtg Val	Arg ttg Leu atc Ile 205 aac	Ile att Ile 190 ctc Leu ata	Ile 175 gga Gly gga Gly gct	Gly caa Gln gag Glu	ser aag Lys cat His gtc Val	Ctt Leu gga Gly 210 cct	Cys ggt Gly 195 gac Asp	Asn 180 atc Ile tca ser	cat His agt Ser	tct ser gtt Val ctg Leu	Xaa gaa Glu cct Pro 215 aac	Ala agc ser 200 gtg Val tct	Arg 185 tgc Cys tgg Trp	Phe cat His agt Ser	Arg gga Gly gga Gly gga Gly	781 829
ttc Phe tgg Trp gtg Val 220	ttg Leu atc Ile 205 aac Asn	att Ile 190 ctc Leu ata Ile	Ile 175 gga Gly gga Gly gct Ala	caa Gln gag Glu ggt Gly	ser aag Lys cat His gtc Val 225	Cly Ctt Leu gga Gly 210 Cct Pro	Cys ggt Gly 195 gac Asp ttg Leu	Asn 180 atc Ile tca ser aag Lys	cat His agt Ser gat Asp	tct ser gtt Val ctg Leu 230	Xaa gaa Glu cct Pro 215 aac Asn	agc Ser 200 gtg Val tct Ser	Arg 185 tgc Cys tgg Trp gat Asp	Phe cat His agt Ser ata Ile	Arg gga Gly gga Gly gga Gly 235	781 829 877
Asn ttc Phe tgg Trp gtg Val 220 act	ttg Leu atc Ile 205 aac Asn	att Ile 190 ctc Leu ata Ile	Ile 175 gga Gly gga Gly gct Ala	caa Gln gag Glu ggt Gly cct	ser aag Lys cat His gtc Val 225 gag	Ctt Leu gga Gly 210 cct Pro	Cys ggt Gly 195 gac Asp ttg Leu	Asn 180 atc Ile tca ser aag Lys	cat His agt Ser gat Asp	tct ser gtt Val ctg Leu 230 gtc	Xaa gaa Glu cct Pro 215 aac Asn cac	Ala agc ser 200 gtg Val tct ser aaa	Arg 185 tgc Cys tgg Trp gat Asp	Phe cat His agt ser ata Ile gtg	Arg gga Gly gga Gly gga Gly 235 act	781 829
Asn ttc Phe tgg Trp gtg Val 220 act	ttg Leu atc Ile 205 aac Asn	att Ile 190 ctc Leu ata Ile	Ile 175 gga Gly gga Gly gct Ala	caa Gln gag Glu ggt Gly cct	ser aag Lys cat His gtc Val 225 gag	Ctt Leu gga Gly 210 cct Pro	Cys ggt Gly 195 gac Asp ttg Leu	Asn 180 atc Ile tca ser aag Lys	cat His agt Ser gat Asp	tct ser gtt Val ctg Leu 230 gtc	Xaa gaa Glu cct Pro 215 aac Asn cac	Ala agc ser 200 gtg Val tct ser aaa	Arg 185 tgc Cys tgg Trp gat Asp	Phe cat His agt Ser ata Ile	Arg gga Gly gga Gly gga Gly 235 act	781 829 877
Asn ttc Phe tgg Trp gtg Val 220 act Thr	ttg Leu atc Ile 205 aac Asn gat Asp	Ile att Ile 190 ctc Leu ata Ile aaa Lys	Ile 175 9ga Gly gga Gly gct Ala gat Asp	Gly caa Gln gag Glu ggt Gly cct Pro 240	ser aag Lys cat His gtc Val 225 gag Glu	Gly ctt Leu gga Gly 210 cct Pro caa Gln	Cys ggt Gly 195 gac Asp ttg Leu tgg Trp	Asn 180 atc Ile tca Ser aag Lys	cat His agt Ser gat Asp aat Asn 245	tct Ser gtt Val ctg Leu 230 gtc Val	Xaa gaa Glu cct Pro 215 aac Asn cac	Ala agc Ser 200 gtg Val tct Ser aaa Lys	Arg 185 tgc Cys tgg Trp gat Asp	Phe cat His agt Ser ata Ile gtg Val 250	Arg gga Gly gga Gly gga Gly 235 act Thr	781 829 877 925
Asn ttc Phe tgg Trp gtg Val 220 act Thr	ttg Leu atc Ile 205 aac Asn gat Asp	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc	Ile 175 gga Gly ggt Ala gat Asp	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag	ser aag Lys cat His gtc Val 225 gag Glu att	Gly ctt Leu gga Gly 210 cct Pro caa Gln att	Cys ggt Gly 195 gac Asp ttg Leu tgg Trp	Asn 180 atc Ile tca Ser aag Lys aaa Lys	Leu cat His agt Ser gat Asp aat Asn 245 aaa	tct ser gtt Val ctg Leu 230 gtc Val	Xaa gaa Glu cct Pro 215 aac Asn cac His	Ala agc Ser 200 gtg Val tct Ser aaa Lys act	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu	Phe cat His agt Ser ata Ile gtg Val 250 tgg	Arg gga Gly gga Gly 235 act Thr	781 829 877
Asn ttc Phe tgg Trp gtg Val 220 act Thr	ttg Leu atc Ile 205 aac Asn gat Asp	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc	Ile 175 9ga Gly gga Gly gct Ala gat Asp	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag	ser aag Lys cat His gtc Val 225 gag Glu att	Gly ctt Leu gga Gly 210 cct Pro caa Gln att	Cys ggt Gly 195 gac Asp ttg Leu tgg Trp	Asn 180 atc Ile tca ser aag Lys aaa Lys	Leu cat His agt Ser gat Asp aat Asn 245 aaa	tct ser gtt Val ctg Leu 230 gtc Val	Xaa gaa Glu cct Pro 215 aac Asn cac His	Ala agc Ser 200 gtg Val tct Ser aaa Lys act	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct Ser	Phe cat His agt Ser ata Ile gtg Val 250	Arg gga Gly gga Gly 235 act Thr	781 829 877 925
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala	ttg Leu atc Ile 205 aac Asn gat Asp	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu	ser aag Lys cat His gtc Val 225 gag Glu att Ile	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile	Cys ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys	Asn 180 atc Ile tca ser aag Lys aaa Lys atg Met 260	cat His agt Ser gat Asp aat Asn 245 aaa Lys	tct ser gtt Val ctg Leu 230 gtc Val ggt Gly	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct ser 265	Phe cat His agt Ser ata Ile gtg Val 250 tgg Trp	Arg gga Gly gga Gly 235 act Thr gcc Ala	781 829 877 925
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala	ttg Leu atc Ile 205 aac Asn gat Asp act Thr	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg	ser aag Lys cat His gtc Val 225 gag Glu att Ile	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile	Cys ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys	Asn 180 atc Ile tca ser aag Lys aaa Lys atg Met 260 aca	cat His agt Ser gat Asp aat Asn 245 aaa Lys	tct ser gtt Val ctg Leu 230 gtc Val ggt Gly	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct ser 265 aag	Phe cat His agt ser ata Ile gtg Val 250 tgg Trp aat	Arg gga Gly gga Gly 235 act Thr gcc Ala	781 829 877 925
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala	ttg Leu atc Ile 205 aac Asn gat Asp act Thr	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta Leu	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg	ser aag Lys cat His gtc Val 225 gag Glu att Ile	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile	Cys ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys tta Leu	Asn 180 atc Ile tca ser aag Lys aaa Lys atg Met 260 aca	cat His agt Ser gat Asp aat Asn 245 aaa Lys	tct ser gtt Val ctg Leu 230 gtc Val ggt Gly	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr ttg Leu	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct ser 265 aag	Phe cat His agt Ser ata Ile gtg Val 250 tgg Trp	Arg gga Gly gga Gly 235 act Thr gcc Ala	781 829 877 925
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala att Ile	ttg Leu atc Ile 205 aac Asn gat Asp act Thr	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta Leu 270	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct Ser	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg Val	ser aag Lys cat His gtc Val 225 gag Glu att Ile gcc Ala	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile gat Asp	Gys ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys tta Leu 275	Asn 180 atc Ile tca ser aag Lys aaa Lys atg Met 260 aca Thr	cat His agt Ser gat Asp aat Asn 245 aaa Lys	tct Ser gtt Val ctg Leu 230 gtc Val ggt Gly agt Ser	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr att Ile	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr ttg Leu 280	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct Ser 265 aag Lys	Phe cat His agt Ser ata Ile gtg Val 250 tgg Trp aat Asn	Arg gga Gly gga Gly 235 act Thr gcc Ala ctt Leu	781 829 877 925 973
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala att Ile	ttg Leu atc Ile 205 aac Asn gat Asp act Thr	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta Leu 270 ata	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct ser	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg Val cca	ser aag Lys cat His gtc Val 225 gag Glu att Ile gcc Ala gtt	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile gat Asp	Cys ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys tta Leu 275 acc	Asn 180 atc Ile tca ser aag Lys aaa Lys atg Met 260 aca Thr	Leu cat His agt Ser gat Asp aat Lys gaa Glu act	tct Ser gtt Val ctg Leu 230 gtc Val ggt Gly agt Ser	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr att Ile	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr ttg Leu 280 ctc	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct Ser 265 aag Lys	Phe cat His agt Ser ata Ile gtg Val 250 tgg Trp aat Asn gga	Arg gga Gly gga Gly 235 act Thr gcc Ala ctt Leu ata	781 829 877 925
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala att Ile	ttg Leu atc Ile 205 aac Asn gat Asp act Thr	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta Leu 270 ata	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct ser	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg Val cca	ser aag Lys cat His gtc Val 225 gag Glu att Ile gcc Ala gtt	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile gat Asp	Cys ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys tta Leu 275 acc	Asn 180 atc Ile tca ser aag Lys aaa Lys atg Met 260 aca Thr	Leu cat His agt Ser gat Asp aat Lys gaa Glu act	tct Ser gtt Val ctg Leu 230 gtc Val ggt Gly agt Ser	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr att Ile	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr ttg Leu 280 ctc	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct Ser 265 aag Lys	Phe cat His agt Ser ata Ile gtg Val 250 tgg Trp aat Asn	Arg gga Gly gga Gly 235 act Thr gcc Ala ctt Leu ata	781 829 877 925 973
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala att Ile agg Arg	ttg Leu atc Ile 205 aac Asn gat Asp act Thr ggc Gly aga Arg 285	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta Leu 270 ata Ile	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct Ser cat	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg Val cca Pro	ser aag Lys cat His gtc Val 225 gag Glu att Ile gcc Ala gtt Val	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile gat Asp tcc Ser 290	ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys tta Leu 275 acc Thr	Asn 180 atc Ile tca ser aag Lys aaa Lys atg Met 260 aca Thr ata Ile	cat His agt Ser gat Asp aat Asn 245 aaa Lys gaa Glu act Thr	tct ser gtt Val ctg Leu 230 gtc Val ggt Gly agt ser aag Lys	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr att Ile ggc Gly 295	agc Ser 200 gtg Val tct Ser aaa Lys act Thr ttg Leu 280 ctc Leu	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct Sef5 aag Lys tat	Phe cat His agt Ser ata Ile gtg Val 250 tgg Trp aat Asn gga Gly	gga Gly gga Gly 235 act Thr gcc Ala ctt Leu	781 829 877 925 973 1021 1069
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala att Ile agg Arg	ttg Leu atc Ile 205 aac Asn gat Asp act Thr ggc Gly aga Arg 285 gaa	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta Leu 270 ata Ile gaa	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct Ser cat His	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg Val cca Pro ttc	ser aag Lys cat His gtc Val 225 gag Glu att Ile gcc Ala gtt Val ctc	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile gat Asp tcc ser 290 agt	Gys ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys tta Leu 275 acc Thr	Asn 180 atc Ile tca Ser aag Lys ata Lys atg Met 260 aca Thr ata Ile	cat His agt Ser gat Asp aat Asn 245 aaa Lys gaa Glu act Thr	tct ser gtt Val ctg Leu 230 gtc Val ggt Gly agt ser aag Lys	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr att Ile ggc Gly 295 ctg	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr ttg Leu 280 ctc Leu gga	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct 265 aag Lys tat Tyr	Phe cat His agt Ser ata Ile gtg Val 250 tgg Trp aat Asn gga Gly aac	Arg gga Gly gga Gly 235 act Thr gcc Ala ctt Leu ata Ile	781 829 877 925 973
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala att Ile agg Arg rat Xaa	ttg Leu atc 11e 205 aac Asn gat Asp act Thr ggc aga Arg 285 gaa Glu	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta Leu 270 ata Ile gaa	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct Ser cat His	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg Val cca Pro ttc	ser aag Lys cat His gtc Val 225 gag Glu att Ile gcc Ala gtt Val ctc Leu	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile gat Asp tcc ser 290 agt	Gys ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys tta Leu 275 acc Thr	Asn 180 atc Ile tca Ser aag Lys ata Lys atg Met 260 aca Thr ata Ile	cat His agt Ser gat Asp aat Asn 245 aaa Lys gaa Glu act Thr	tct Ser gtt Val ctg Leu 230 gtc Val ggt Gly agt Ser aag Lys atc	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr att Ile ggc Gly 295 ctg	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr ttg Leu 280 ctc Leu gga	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct 265 aag Lys tat Tyr	Phe cat His agt Ser ata Ile gtg Val 250 tgg Trp aat Asn gga Gly	Arg gga Gly gga Gly 235 act Thr gcc Ala ctt Leu ata Ile ggt Gly	781 829 877 925 973 1021 1069
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala att Ile agg Arg	ttg Leu atc 11e 205 aac Asn gat Asp act Thr ggc aga Arg 285 gaa Glu	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta Leu 270 ata Ile gaa	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct Ser cat His	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg Val cca Pro ttc	ser aag Lys cat His gtc Val 225 gag Glu att Ile gcc Ala gtt Val ctc	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile gat Asp tcc ser 290 agt	Gys ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys tta Leu 275 acc Thr	Asn 180 atc Ile tca Ser aag Lys ata Lys atg Met 260 aca Thr ata Ile	cat His agt Ser gat Asp aat Asn 245 aaa Lys gaa Glu act Thr	tct ser gtt Val ctg Leu 230 gtc Val ggt Gly agt ser aag Lys	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr att Ile ggc Gly 295 ctg	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr ttg Leu 280 ctc Leu gga	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct 265 aag Lys tat Tyr	Phe cat His agt Ser ata Ile gtg Val 250 tgg Trp aat Asn gga Gly aac	Arg gga Gly gga Gly 235 act Thr gcc Ala ctt Leu ata Ile	781 829 877 925 973 1021 1069
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala att Ile agg Arg rat Xaa 300	ttg Leu atc 11e 205 aac Asn gat Asp act Thr ggc Gly aga 285 gaa Glu	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta Leu 270 ata Ile gaa Glu	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct Ser cat His	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg Val cca Pro ttc Phe	ser aag Lys cat His gtc Val 225 gag Glu att Ile gcc Ala gtt Val ctc Leu 305	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile gat Asp tcc Ser 290 agt Ser	ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys tta Leu 275 acc Thr	Asn 180 atc Ile tca Ser aag Lys atg Met 260 aca Thr ata Ile cct Pro	cat His agt Ser gat Asp aat Asn 245 aaa Lys gaa Glu act Thr tgt	tct ser gtt Val ctg Leu 230 gtc Val ggt Gly agt Ser aag Lys atc 11e 310	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr att Ile ggc 295 ctg Leu	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr ttg Leu gga Gly	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct 265 aag Lys tat Tyr	Phe cat His agt Ser ata Ile gtg Val 250 trp aat Asn gga Gly aac Asn	Arg gga Gly gga Gly 235 act Thr gcc Ala ctt Leu ata Ile ggt Gly 315	781 829 877 925 973 1021 1069
Asn ttc Phe tgg Trp gtg Val 220 act Thr gca Ala att Ile agg Arg rat Xaa 300 att	Arg ttg Leu atc 11e 205 aac Asn gat Asp act Thr ggc gly aga Arg 285 gaa Glu acc	Ile att Ile 190 ctc Leu ata Ile aaa Lys gcc Ala cta Leu 270 ata Ile gaa Glu	Ile 175 9ga Gly gct Ala gat Asp tat Tyr 255 tct Ser cat His gtal ctt	Gly caa Gln gag Glu ggt Gly cct Pro 240 gag Glu gtg Val cca Pro ttc Phe ata	ser aag Lys cat His gtc Val 225 gag Glu att Ile gca gtt Val ctc Leu 305 aag	Gly ctt Leu gga Gly 210 cct Pro caa Gln att Ile gat Asp tcc Ser 290 agt Ser ata	Cys ggt Gly 195 gac Asp ttg Leu tgg Trp aaa Lys tta Leu 275 acc Thr att Ile aag	Asn 180 atc Ile tca Ser aag Lys atg Met 260 aca Thr atle cct Pro	Leu cat His agt Ser gat Asp aat Asn 245 aaa Lys gal act Thr tgt Cys acc	Ile tct Ser gtt Val ctg Leu 230 gtc Val ggt Gly agt Ser aag Lys atc Ile 310 cct	Xaa gaa Glu cct Pro 215 aac Asn cac His tat Tyr att Ile ggcy 295 ctg Leu gaa	Ala agc Ser 200 gtg Val tct Ser aaa Lys act Thr ttg Leu gga Gly gaa	Arg 185 tgc Cys tgg Trp gat Asp gaa Glu tct 265 aag Lys tat Tyr gag	Phe cat His agt Ser ata Ile gtg Val 250 tgg Trp aat Asn gga Gly aac	Arg gga Gly gga Gly 235 act Thr gcc Ala ctt Leu ata Ile ggt Gly 315 cat	781 829 877 925 973 1021 1069

<sup>5</sup> 4 320 325 330	
ctg aaa aaa agt gca aaa aca ctc tgg gaa att cag aat aag ctt aag	1213
Leu Lys Lys Ser Ala Lys Thr Leu Trp Glu Ile Gln Asn Lys Leu Lys	
335 340 345	
ctt taaagttgcc taaaactacc attccgaaat tattgaagag atcatagata	1266
Leu	
caggattata taacgaaatt ttgaataaac ttgaattcct aaaagatgga aacaggaaag	1326
taggtagagt gattttccta tttatttagt cctccagctc ttttattgag catccacgtg	1386
ctggacgata cttatttaca attcckaagt atttttggta cctctgatgt agcagcactt	1446
gccatgttat atatatgtag ttgrmatttg gttcccaaaa agtaggatgt aggtatttat	1506
tgtgttctag aaattccgac tcttttcatt agatatatgc tatttctttc attcttgctg	1566
gtttatacct atgttcattt atatgctgta aaaaagtagt agcttcttct acaatgtaaa	1626
aataaatgta catacaaaaa aaaaaamcmc	1656
ancadacyca cacacadada dadadamente	2000
<210> 308	
<211> 517	
·	
<212> DNA	
<213> Homo sapiens	
	•
<220>	
<221> CDS	
<222> 48164	
<221> sig_peptide	
<222> 4889	
<223> Von Heijne matrix	
score 4	
score 4 seq YYMVCLFFRLIFS/EH	
score 4 seq YYMVCLFFRLIFS/EH <221> polyA_signal	
score 4 seq YYMVCLFFRLIFS/EH	
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487	,
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site	
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487	
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site	
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site	
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517	56
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308	
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac	56
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr	
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att	
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile	
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile -10 -5 1 5	104
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile -10 -5 ata ggc act gtc act tct cac aaa act ggg aca cta act gtt tat cca	104
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile -10 -5 1 5 ata ggc act gtc act tct cac aaa act ggg aca cta act gtt tat cca Ile Gly Thr Val Thr Ser His Lys Thr Gly Thr Leu Thr Val Tyr Pro 10 15 20	104
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatage ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile -10 -5 1 5 ata ggc act gtc act tct cac aaa act ggg aca cta act gtt tat cca Ile Gly Thr Val Thr Ser His Lys Thr Gly Thr Leu Thr Val Tyr Pro 10 15 20 aca tct gct ggc taaataaaga catgatcttc accttttggg attgttaatt	104 152
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile -10 -5 1 5 ata ggc act gtc act tct cac aaa act ggg aca cta act gtt tat cca Ile Gly Thr Val Thr Ser His Lys Thr Gly Thr Leu Thr Val Tyr Pro 10 15 20	104 152
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile -10 -5 ata ggc act gtc act tct cac aaa act ggg aca cta act gtt tat cca Ile Gly Thr Val Thr Ser His Lys Thr Gly Thr Leu Thr Val Tyr Pro 10 15 20 aca tct gct ggc taaataaaga catgatcttc accttttggg attgttaatt Thr Ser Ala Gly 25	104 152
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatage ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile -10 -5 ata ggc act gtc act tct cac aaa act ggg aca cta act gtt tat cca Ile Gly Thr Val Thr Ser His Lys Thr Gly Thr Leu Thr Val Tyr Pro 10 15 20 aca tct gct ggc taaataaaga catgatcttc accttttggg attgttaatt Thr Ser Ala Gly 25 taaaatggtt ccataagagc aatgcaaaga cagagatatt tggcagcact gcagctggtg	104 152 204
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatage ctegtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile -10 -5 1 5 ata ggc act gtc act tct cac aaa act ggg aca cta act gtt tat cca Ile Gly Thr Val Thr Ser His Lys Thr Gly Thr Leu Thr Val Tyr Pro 10 15 20 aca tct gct ggc taaataaaga catgatctc accttttggg attgttaatt Thr Ser Ala Gly 25 taaaatggtt ccataagagc aatgcaaaga cagagatatt tggcagcact gcagctggtg atttatatgg ctcttcacaa ggtgttattt tgggggtatca aggtatggat gcttaaatca	104 152 204 264 324
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile -10 -5 1 5 ata ggc act gtc act tct cac aaa act ggg aca cta act gtt tat cca Ile Gly Thr Val Thr Ser His Lys Thr Gly Thr Leu Thr Val Tyr Pro 10 15 20 aca tct gct ggc taaataaaga catgatcttc accttttggg attgttaatt Thr Ser Ala Gly 25 taaaatggtt ccataagagc aatgcaaaga cagagatatt tggcagcact gcagctggtg atttatatgg ctcttcacaa ggtgttattt tggggtatca aggtatggat gcttaaatca gctgcaggaa gtaagaaaga agaaaaaagg agtgataaag ataaaaaaaa	104 152 204 264 324 384
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac	104 152 204 264 324 384 444
score 4 seq YYMVCLFFRLIFS/EH  <221> polyA_signal <222> 482487  <221> polyA_site <222> 505517  <400> 308 aggagatagc ctcgtagaaa tgacaaccac aatgttaata ctaacat atg tat tac Met Tyr Tyr atg gtt tgt ttg ttc ttt cgc tta ata ttt tca gag cac cta cct att Met Val Cys Leu Phe Phe Arg Leu Ile Phe Ser Glu His Leu Pro Ile -10 -5 1 5 ata ggc act gtc act tct cac aaa act ggg aca cta act gtt tat cca Ile Gly Thr Val Thr Ser His Lys Thr Gly Thr Leu Thr Val Tyr Pro 10 15 20 aca tct gct ggc taaataaaga catgatcttc accttttggg attgttaatt Thr Ser Ala Gly 25 taaaatggtt ccataagagc aatgcaaaga cagagatatt tggcagcact gcagctggtg atttatatgg ctcttcacaa ggtgttattt tggggtatca aggtatggat gcttaaatca gctgcaggaa gtaagaaaga agaaaaaagg agtgataaag ataaaaaaaa	104 152 204 264 324 384

<211> 405

<212> DNA

<213> Homo sapiens

```
<220>
<221> CDS
<222> 185..334
<221> sig_peptide
<222> 185..295
<223> Von Heijne matrix
      score 5.90000009536743
      seq LSYASSALSPCLT/AP
<221> polyA_signal
<222> 355..360
<221> polyA site
<222> 392..405
<400> 309
atcaccttct totocatcct tstotgggcc agtococarc coagtocotc tootgacctg
                                                                      . 60
                                                                      120
cccaqcccaa qtcaqccttc aqcacqcqct tttctgcaca cagatattcc aggcctacct
ggcattccag gacctccgma atgatgctcc agtcccttac aagcgcttcc tggatgaggg
                                                                      180
tggc atg gtg ctg acc acc ctc ccc ttg ccc tct gcc aac agc cct gtg
                                                                      229
     Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val
                                 -30
             -35
aac atg ccc acc act ggc ccc aac agc ctg agt tat gct agc tct gcc
                                                                      277
Asn Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala
        -20
                            -15
                                                                      325
ctg tcc ccc tgt ctg acc gct cca aag tcc ccc cga ctt gct atg atg
Leu Ser Pro Cys Leu Thr Ala Pro Lys Ser Pro Arg Leu Ala Met Met
    -5
                        1
                                                                      374
cct gac aac taaatatcct tatccaaatc aataaarwra raatcctccc
Pro Asp Asn
                                                                      405
tccaraaggg tttctaaaaa caaaaaaaa a
<210> 310
<211> 1087
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 195..347
<221> sig peptide
<222> 195..272
<223> Von Heijne matrix
      score 7.09999990463257
      seq LASLQWSLTLAWC/GS
<221> polyA_signal
<222> 1037..1042
<221> polyA_site
<222> 1071..1082
<400> 310
aaagtgtaga acacggacct ctgagttatg ctcttgagag gtgccaaagc tgggctgttt
                                                                        60
                                                                       120
acctacctta tccacagage tetgaaagte aagecagaaa ggaaggatte caaattettg
gaattttatc tagaaaagaa gactaagcag cttttgttct tctgtgaccc agttgctggc
                                                                       180
ccaagacatg gaca atg acc ccc tgg tgt ttg gcg tgt ctg ggg agg agg
                                                                       230
```

·	
Met Thr Pro Trp Cys Leu Ala Cys Leu Gly Arg Arg	
	278
cet ete get tet ttg eag tgg age etg aca etg geg tgg tgt gge tee	2/0
Pro Leu Ala Ser Leu Gln Trp Ser Leu Thr Leu Ala Trp Cys Gly Ser	
-10 -5 1	
ggc agc cac tgg aca gag aga cca akt cag akt tca ccg tgg akt tct	326
Gly Ser His Trp Thr Glu Arg Pro Xaa Gln Xaa Ser Pro Trp Xaa Ser	
5 10 15	
ctg tca gcg acc acc agg ggg tgatcacacg gaaggtgaac atccaggtcg	377
Leu Ser Ala Thr Thr Arg Gly	
20 25	
gggatgtgaa tgacaacgcg cccacatttc acaatcagcc ctacagcgtc cgcatccctg	437
araatacacc agtggggacg cccatcttca tcgtgaatgc cacagacccc gacttggggg	497
cagggggcag cgtcctctac tccttccagc cccctccca attcttcgcc attgacagcg	557
cccgcggtat cktcacagtg atccgggagc tggactacga taccacrcmg gcctaccagc	617
	677
towoggtowa ogcoacagat caagacaara coaggootot gtocacostg gocaacttgg	737
ccatcatcat cacagatgte caggacatgg accecatett catcaacetg cettacagea	
ccaacatcta cgagcattct cctccgggca cgacggtgcg catcatcacc gccatagacc	797
aggataaagg acgtccccgg ggcattggct acaccatcgt ttcagggcat ctgtgtttac	857
aagaacccaa gatctctcag gagctcagga aaaggggctt gctgtgaggc tcagggttcc	917
catggacatt ctgagctgac cctcctcagc attggatctc ctggctcagg aactaggaac	977
gaagettgga tgttttetee ttteetacag catetgtatt cattteetat agttgecata	1037
ataaaatgcc actaacttag tggcttaaaa accaaaaaaa aaaaaccctt	1087
<210> 311	
<211> 916	
<212> DNA	
<213> Homo sapiens	
42107 Hollio Baptella	
<220>	
<221> CDS	
· · · · · · · · · · · · · · · · · · ·	
<222> 90815	
<221> sig_peptide	
<222> 90179	
<223> Von Heijne matrix	
score 13.1999998092651	
seq LLLLSTLVIPSAA/AP	
,	
<221> polyA_signal	•
<222> 883888	
<221> polyA_site	
<222> 905 <del>9</del> 16	
<400> 311	
aaaacagtac gtgggcggcc ggaatccggg agtccggtga cccgggctgt ggtctagcat	60
aaaggcggag ccagaagaag gggcggggt atg gga gaa gcc tcc cca cct gcc	113
Met Gly Glu Ala Ser Pro Pro Ala	
-30 -25	
	161
ccc gca agg cgg cat ctg ctg gtc ctg ctg ctc ctc tct acc ctg	101
Pro Ala Arg Arg His Leu Leu Val Leu Leu Leu Leu Ser Thr Leu	
-20 -15 -10	
gtg atc ccc tcc gct gca gct cct atc cat gat gct gac gcc caa gag	209
Val Ile Pro Ser Ala Ala Ala Pro Ile His Asp Ala Asp Ala Gln Glu	
-5 1 5 10	
ago too ttg ggt oto aca ggo oto cag ago ota oto caa ggo tto ago	257
Ser Ser Leu Gly Leu Thr Gly Leu Gln Ser Leu Leu Gln Gly Phe Ser	
15 20 25	

cga ctt ttc ctg aaa ggt aac ctg ctt cgg ggc ata gac agc tta ttc

305

Arg	Leu	Phe	Leu 30	Lys	Gly	Asn	Leu	Leu 35	Arg	Gly	Ile	Asp	Ser 40	Leu	Phe		
	gcc Ala		_	_											-		353
	aac Asn 60																401
	atc Ile																449
	aat Asn																497
<del>-</del>	ttg Leu	Lys	-														545
	aag Lys																593
	tgg Trp 140			_													641
	ggc Gly																689
cgg	gat Asp																<b>737</b>
	gar Glu	_						_			_						785
-	tac Tyr		ctc	_				cag	_	tar	gggt	ggg (	gacc	<b>3</b> 999	ar		835
	ctgc acat	ctg				arac		c cc	caag	cacc	ata	tgga	aat a	aaag	ttcttt	=	895 916

<211> 583

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 52..513

<221> sig\_peptide

<222> 52..231

<223> Von Heijne matrix score 4 seq LVRRTLLVAALRA/WM

<221> polyA\_signal

<222> 553..558

<221> polyA\_site

<222> 572..583

<400> 312

aagg	aaad	cag (	caaco	cagag	gg ga	agato	gatca	a <sub>,</sub> cct	gaad	ccac	tgct	ccaa	aac (		g ggc : Gly	57	,
													gaa Glu -45			105	;
		_	_	_			_		_			_	aaa Lys		-	153	ţ
	-	_		_		_	-			_		-	ctg Leu		_	201	L
		_	_	_	_	_			_		_		cag Gln	_		249	)
													cag Gln 20			<b>297</b>	,
													ctc Leu			345	;
Cys		-	_		_	_			_		_		atg Met	_		393	}
_		_	_		_	_			-	_		_	ttc Phe			441	L
													cag Gln			489	)
				atc		tca Ser		tgaa	aaggo	cct o	9999	catg	ga ga	aaca	ggctg	543	3
cact	acc	cta a		atgt	ct ga	acca	ggta	a aaa	aaaa	aaaa						583	3

<211> 697

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 172..438

<221> sig\_peptide

<222> 172..354

<223> Von Heijne matrix
 score 4.69999980926514
 seq LLPCNLHCSWLHS/SP

<221> polyA\_signal

<222> 682..687

<221> polyA\_site

<222> 685..697

<400> 313

agattggctg ggcagatggg ctgactggct gggcagatgg gtgggtgagt tccctctccc 60 cagagccatc ggccaggtac caaagctcag ctgtatggat tcccaacagg aggacctgcg 120 cttccctggg acccattgtt gtactggatt aacaagcgac ggcgctacgg c atg aat 177

Met Asn	
gca gcc atc aac acg ggc cct gcc cct gct gtc acc aag act gag act Ala Ala Ile Asn Thr Gly Pro Ala Pro Ala Val Thr Lys Thr Glu Thr -55 -50 -45	225
gag gtc cag aat cca gat gtt ctg tgg gat ttg gac atc ccc gaa gcc Glu Val Gln Asn Pro Asp Val Leu Trp Asp Leu Asp Ile Pro Glu Ala -40 -35 -30	273
agg agc cat gct gac caa gac agc aac ccc aag gcg gaa gcc ctg ctc Arg Ser His Ala Asp Gln Asp Ser Asn Pro Lys Ala Glu Ala Leu Leu -25 -20 -15	321
CCC tgc aac ctg cac tgc agc tgg ctc cac agc agc ccc agg cca gat Pro Cys Asn Leu His Cys Ser Trp Leu His Ser Ser Pro Arg Pro Asp -10 -5 1 5	369
ccc cat tcc cac ttc cca tct ktc agg agg tgc cct ttg ccc cac cct Pro His Ser His Phe Pro Ser Xaa Arg Arg Cys Pro Leu Pro His Pro 10 15 20	417
tgt gca acc tac ccc ccs kgc tgaaccactc tgtctcctat cctttggcca Cys Ala Thr Tyr Pro Pro Xaa 25	468
cctgtcctga aaggaatgtt ctcttccatt ccctcctgaa tctggcccag gaagaccata gcttcaatgy caagcctttt ccttcaaaac tgtagcctcc tctcactgaa ggtgggagct	528 588
gcaggaatca ggtgcagagt aggaaatgga actaacctca ggaaggtggt attgacagag gtcaggaccc acctggatgt catgctatga aacattaaaa gaaaaaaaa	648 697
.210. 214	
<210> 314 <211> 803	
<212> DNA <213> Homo sapiens	
<220> <221> CDS	
<222> 148366	
<221> sig_peptide	
<222> 148225 <223> Von Heijne matrix	
score 5.5 seq LFTLLFLIMLVLK/LD	
<221> polyA_signal	
<222> 770775	
<221> polyA_site <222> 792803	
<400> 314 aaatgggggg aaaagggcgg aaaaggacaa ggatccaaac tggcgaattt gctgatcttc	60
gcgtccctct ccgctttccg gccggcagcg ctgccagggt atatttcctt ttttccgatc ctgcaacagc ctctttaaac tgtttaa atg aga atg tcc ttg gct cag aga gta  Met Arg Met Ser Leu Ala Gln Arg Val	120 174
-25 -20 cta ctc acc tgg ctt ttc aca cta ctc ttc ttg atc atg ttg gtg ttg	222
Leu Leu Thr Trp Leu Phe Thr Leu Leu Phe Leu Ile Met Leu Val Leu -15 -10 -5	
aaa ctg gat gag aaa gca cct tgg aac tgg ttc ctc ata ttc att cca Lys Leu Asp Glu Lys Ala Pro Trp Asn Trp Phe Leu Ile Phe Ile Pro	270
gto tgg ata ttt gat act atc ctt ctt gto ctg ctg att gtg aaa atg	318
Val Trp Ile Phe Asp Thr Ile Leu Leu Val Leu Leu Ile Val Lys Met	

<sup>1</sup> 20 25 30	
gct ggg cgg tgt aag tct ggc ttt gac ctc gac atg gat cac aca ata	366
Ala Gly Arg Cys Lys Ser Gly Phe Asp Leu Asp Met Asp His Thr Ile	
35 40 45	
taaaaaaaaa aacctggtac ctcattgcac tgtkacttaa attasccttc tgcctcgcac	426
tctgtgctaa actggaacag tttactacca tgaatctatc ctatgtcttc attcctttat	486
gggccttgct ggctggggct ttaacagaac tcggatataa tgtctttttt gtgaaagact	546
gacttctaag tacatcatct cctttctatt gctgttcaac aagttaccat taaagtgttc	606
tgaatctgtc aagcttcaag aataccagag aactgaggga aaataccaaa tgtagtttta	666
tactacttcc ataaaacagg attggtgaat cacggacttc tagtcaacct acagcttaat	726
tattcagcat ttgagttatt gaaatcctta ttatctctat gtaaataaag tttgttttgg	786
acctcaaaaa aaaaaaa	803
<210> 315	
<211> 823	
<212> DNA	
<213> Homo sapiens	
-200	
<220>	•
<pre>&lt;221&gt; CDS -&lt;222&gt;-175336</pre>	
<2225 175336	
<221> sig_peptide	
<222> 175276	
<223> Von Heijne matrix	
score 3.7000004768372	
seg SVLNVGHLLFSSA/CS	
bed by my committees, es	
<221> polvA site	
<221> polyA_site	
<221> polyA_site <222> 812823	•
<222> 812823 <400> 315	60
<222> 812823  <400> 315 aaggegegeg egaceggegg etetteggeg eggattaggg ggteteggeg agggagteat	60 120
<222> 812823 <400> 315	
<222> 812823  <400> 315 aaggegege egaceggeg etetteggeg eggattaggg ggteteggeg agggagteat caagettegg egtatget ggeeggtet gaagteteg agaagetetg etgaggaaga	120
<222> 812823  <400> 315  aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg	120
<222> 812823  <400> 315  aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg Met	120 177
<222> 812823  <400> 315  aaggcgcgc cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg  Met atc cct ctg ata agc cac ctt gcc gag gct gct cct cct acc tca tgg	120 177
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273 321
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggegegeg cgaccggegg ctctttggeg cggattaggg ggtcteggeg agggagteat caagetttgg tgtatgtgtt ggeeggttet gaagtettga agaagetetg etgaggaaga ccaaageage actegttgee aattagggaa tggaccgttt gggtteettt agea atg</pre>	120 177 225 273 321 376
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273 321 376
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273 321 376 436 496
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273 321 376 436 496 556
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273 321 376 436 496 556 616
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273 321 376 436 496 556 616 676
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273 321 376 436 496 556 616 676 736
<pre>&lt;222&gt; 812823  &lt;400&gt; 315 aaggcgcgcg cgaccggcgg ctctttggcg cggattaggg ggtctcggcg agggagtcat caagctttgg tgtatgtgtt ggccggttct gaagtcttga agaagctctg ctgaggaaga ccaaagcagc actcgttgcc aattagggaa tggaccgttt gggttccttt agca atg</pre>	120 177 225 273 321 376 436 496 556 616 676

```
<211> 823
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 191..553
<221> sig peptide
<222> 191..304
<223> Von Heijne matrix
      score 5.69999980926514
      seg LAFLSCLAFLVLD/TQ
<221> polyA signal
'<222> 766..771
<221> polyA site
<222> 804..817
<400> 316
aactctgcag ggcctccaag gccaggcttc agggctggga ctcagtcctg aggcactggg
gagccatgag gggctgtggc agggagggc agggtgtgga aagactcccc tggggccatg
                                                                      120
gtggagatgt gctgaggtct tctccctgat cgtcttctcc tccctgctga ccgacggcta
                                                                      180
ccagaackag atg gag tot ceg cag otc cac tgc att otc aac agc aac
                                                                      229
           Met Glu Ser Pro Gln Leu His Cys Ile Leu Asn Ser Asn
                        -35
                                                                      277
age gtg gee tge age ttt gee gtg gga gee gge tte etg gee tte etc
Ser Val Ala Cys Ser Phe Ala Val Gly Ala Gly Phe Leu Ala Phe Leu
                    -20
                                                             -10
                                         -15
ago tgo otg goo tto oto gto otg gao aca cag gag aco ogo att goo
                                                                      325
Ser Cys Leu Ala Phe Leu Val Leu Asp Thr Gln Glu Thr Arg Ile Ala
                -5
                                     1
ggc acc cgc ttc aag aca gcc ttc cag ctc ctg gac ttc atc ctg gct
                                                                      373
Gly Thr Arg Phe Lys Thr Ala Phe Gln Leu Leu Asp Phe Ile Leu Ala
                            15
gtt ctc tgg gca gtt gtc tgg ttc atg ggt ttc tgc ttc ctg gcc aac
                                                                      421
Val Leu Trp Ala Val Val Trp Phe Met Gly Phe Cys Phe Leu Ala Asn
                         30
caa tgg cag cat tcg ccg ccc aaa gar kkc ctc ctg ggg agc agc agt
                                                                      469
Gln Trp Gln His Ser Pro Pro Lys Glu Xaa Leu Leu Gly Ser Ser Ser
                    45
                                         50
ged dag ged ace age stt dad ott ott ote dat oot tigt otig gat
                                                                      517
Ala Gln Ala Ile Gly Xaa His Leu Leu His Pro Cys Leu Asp
                60
                                     65
att cca rgc cta cct ggc akk cca gga cct ccg aaa tgatgctcca
                                                                      563
Ile Pro Xaa Leu Pro Gly Xaa Pro Gly Pro Pro Lys
            75
                                 80
gtcccttacm aregettect ggatgaaggt ggcatggtgs kkaacaccct ccccttgccc
                                                                      623
totgocaaca gootgtgaac atgoccacca otggocccaa cagootgagt tatgotagot
                                                                      683
etgecetgte eccetgtetg accgetemaa agtececeg gettgetatg atgeetgaca
                                                                      743
actaaatato ottatooaaa toaataaaga gagaatooto ootooagaag ggtttotaaa
                                                                      803
aacaaaaaa aaaahncctt
                                                                      823
```

<211> 1112

<212> DNA

<213> Homo sapiens

<221> CDS <222> 106..603 <221> sig\_peptide <222> 106..216 <223> Von Heijne matrix score 4.30000019073486 seq LWEKLTLLSPGIA/VT <221> polyA\_site <222> 1102..1112 . , <400> 317 60 agegattgcg aatceteege tgaggtgatt tggatateee tagaacgttg agggeacgag tegggteetg agaccaggte etcagecage agagecaegt teett atg age ace gtg 117. Met Ser Thr Val ggt tta ttt cat ttt cct aca cca ctg acc cga ata tgc ccg gcg cca 165 Gly Leu Phe His Phe Pro Thr Pro Leu Thr Arg Ile Cys Pro Ala Pro -30 -25 tgg gga ctc cgg ctt tgg gag aag ctg acg ttg tta tcc cca gga ata 213 Trp Gly Leu Arg Leu Trp Glu Lys Leu Thr Leu Leu Ser Pro Gly Ile -15 -10 gct gtc act ccg gtc cag atg gca ggc aag aag gac tac cct gca ctg Ala Val Thr Pro Val Gln Met Ala Gly Lys Lys Asp Tyr Pro Ala Leu 10 ctt tcc ttg gat gag aat gaa ctc gaa gag cag ttt gtg aaa gga cac 309 Leu Ser Leu Asp Glu Asn Glu Leu Glu Glu Gln Phe Val Lys Gly His 20 ggt cca ggg ggc cag gca acc aac aaa acc agc aac tgc gtg gtg ctg Gly Pro Gly Gly Gln Ala Thr Asn Lys Thr Ser Asn Cys Val Val Leu 40 aar mac atc ccc tca ggc atc gtt gta aag tgc cat cag aca aga tca 405 Lys Xaa Ile Pro Ser Gly Ile Val Val Lys Cys His Gln Thr Arg Ser 50 55 gtt gat cag aac aga aag cta gct cgg aaa atc cta caa gag aaa gta 453 Val Asp Gln Asn Arg Lys Leu Ala Arg Lys Ile Leu Gln Glu Lys Val 70 75 rat gtt ttc tac aat ggt gaa aac agt cct gtt cac aaa gaa aaa cga 501 Xaa Val Phe Tyr Asn Gly Glu Asn Ser Pro Val His Lys Glu Lys Arg 85 90 gaa gcg gcg aag aaa aaa car gaa agg aaa aaa aga gca aag gaa acc 549 Glu Ala Ala Lys Lys Gln Glu Arg Lys Lys Arg Ala Lys Glu Thr 100 105 ctg gaa aaa aag aas ctm ctt aaa raa ctg tgg gag tca agt aaa aag 597 Leu Glu Lys Lys Xaa Leu Leu Lys Xaa Leu Trp Glu Ser Ser Lys Lys 115 120 gtc cac tgagaaaaga attagagatt ccaactgaca gaatctgcca gaagctccca 653 gggaataatg gtggcgagtt ccatcaccag cattattata gtgcttcaaa agaaatattt ttgatgaact taaaagacaa caaatttatt taaatggtgc actaaactgt agtgaacaga 773 gacatgcacg attcaagaat aaaactcggc cgggcacggt ggacggtgcc tcacatctgt 833

aatcccagca ctttgggagg ccgaggcggg cggatcactt gaggtcagga gtttgagacc agcctggcca acatggtgaa accccgtctc tactaaaaat acaaaaaatt agccaggcat

ggtggcgggc acctgtaatc ccagctactc gggaggccga ggcaggagaa ttgcgtgaac

ctgggaggcg gaggttgcag tgagctgaga tcgcgccact gcactcaagc ctgggcaaca

cctgggtgac agagcaagac cccatcycaa aaaaaaaaa

893

953

1013

1073 1112

```
<212> DNA
<213> Homo säpiens
<220>
<221> CDS
<222> 47..586
<221> sig_peptide
<222> 47..124
<223> Von Heijne matrix
      score 6.30000019073486
      seq GVGLVTLLGLAVG/SY
<221> polyA_signal
<222> 1583..1588
<221> polyA_site
<222> 1614..1623
<400> 318
agggatetgt eggettgtea ggtggtggag gaaaaggege teegte atg ggg ate
                                                    Met Gly Ile
                                                        -25
                                                                      103
cag acg age ecc gte etg etg gee tee etg ggg gtg ggg etg gte act
Gln Thr Ser Pro Val Leu Leu Ala Ser Leu Gly Val Gly Leu Val Thr
                                -15
ctg ctc ggc ctg gct gtg ggc tcc tac ttg gtt cgg agg tcc cgc cgg
                                                                       151
Leu Leu Gly Leu Ala Val Gly Ser Tyr Leu Val Arg Arg Ser Arg Arg
                                                                       199
cct cag gtc act ctc ctg gac ccc aat gaa aag tac ctg cta cga ctg
Pro Gln Val Thr Leu Leu Asp Pro Asn Glu Lys Tyr Leu Leu Arg Leu
                                         20
                     15
                                                                       247
cta gac aag acg act gtg agc cac aac acc aag agg ttc cgc ttt gcc
Leu Asp Lys Thr Thr Val Ser His Asn Thr Lys Arg Phe Arg Phe Ala
                 30
                                                                       295
ctg ccc acc gcc cac cac act ctg ggg ctg cct gtg ggc aaa cat atc
Leu Pro Thr Ala His His Thr Leu Gly Leu Pro Val Gly Lys His Ile
                                 50
                                                                       343
tac ctc tcc acm mga att gat ggc agc ctg gtc atc agg cca tac act
Tyr Leu Ser Thr Arg Ile Asp Gly Ser Leu Val Ile Arg Pro Tyr Thr
                             65
                                                                       391
cct gtc acc agt gat gag gat caa ggc tat gtg gat ctt gtc mtc aag
Pro Val Thr Ser Asp Glu Asp Gln Gly Tyr Val Asp Leu Val Xaa Lys
                         80
                                                                       439
gtc tac ctg aag ggt gtg cac ccc aaa ttt cct gag gga ggg aar atg
Val Tyr Leu Lys Gly Val His Pro Lys Phe Pro Glu Gly Gly Lys Met
                                         100
                     95
                                                                       487
 tct cak tac ctg gat asc ctg aaa gtt ggg gat btg gtg gaa ttt csg
 Ser Xaa Tyr Leu Asp Xaa Leu Lys Val Gly Asp Xaa Val Glu Phe Xaa
                                     115
                 110
 ggg cca agc ggg ttg ctc act tac act gga aaa ggg cat ttt aac att
                                                                       535
 Gly Pro Ser Gly Leu Leu Thr Tyr Thr Gly Lys Gly His Phe Asn Ile
                                 130
                                                                       583
 cag ccc aac aag aat ctc cac cag aac ccc gag tgg cga aga aac tgg
 Gln Pro Asn Lys Asn Leu His Gln Asn Pro Glu Trp Arg Arg Asn Trp
                             145
                                                                       636
 gaa tgattgccgg cgggacagga atcaccccaa tgctacagct gatccgggcc
 Glu
                                                                       696
 atcctgaaag tccctgaaga tccaacccag tgctttctgc tttttgccaa ccagacagaa
                                                                       756
 aaggatatca tettgeggga ggaettagag gaactgeagg ceegetatee caategettt
                                                                       816
 aagetetggt teactetgga teatececea aaagrttggg cetacageaa gggetttgtg
                                                                       876
 actgccgacw tgatccggga acacctgccc gctccagggg atgatgtct ggtactgctt
```

tgtgggccmc ccccaatggt gcagctggcc tgccatccca acttggacaa actgggctac

```
996
tcacaaaaga tgcgattcac ctactgagca tcctccagct tccctggtgc tgttcgctgc
agttgttccc catcagtact caagcactak aagccttagr ktcctktcct cagagtttca
                                                                     1056
ggttttttca gttrsatcka gagctgaaat ctggatagta cctgcaggaa caatattcct
                                                                     1116
gtagccatgg aagagggcca aggctcagtc actccttgga tggcctccta aatctccccg
                                                                     1176
tggcaacagg tccaggagag gcccatggag cagtctcttc catggagtaa gaaggaaggg
agcatgtacg cttggtccaa gattggctag ttccttgata gcatcttact ctcaccttct
                                                                     1296
ttgtgtctgt gatgaaagga acagtctgtg caatgggttt tacttaaact tcactgttca
                                                                     1356
                                                                     1416
acctatgage aaatetgtat gtgtgagtat aagttgagea tageataett ceagaggtgg
tcttatggag atggcaagaa aggaggaaat gatttcttca gatctcaaag gagtctgaaa
                                                                     1476
tatcatattt ctgtgtgtgt cdctctcagc ccctgcccad gctagaggga wacagctact
                                                                     1536
gataatcgaa aactgctgtt tgtgggcarg aacccctggc tgtgcaaata atggggctga
                                                                     1596
ngccctgtgt gatattgaaa aaaaaaa
                                                                     1623
<210> 319
<211> 526
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 99..371
<221> sig_peptide
<222> 99..290
<223> Von Heijne matrix
      score 3.79999995231628
      seg LFIVVCVICVTLN/FP
<221> polyA_signal
<222> 491..496
<221> polyA site
<222> 513..524
<400> 319
attggattag tagaattgct tttgtcattc cattgttttc atatatttgt ttgggacatt
                                                                       60
ttactttttt ctgttaacgc ttaccctagr aattagaa atg aca cca cgt att ctt
                                                                      116
                                           Met Thr Pro Arg Ile Leu
age gaa gte cag ttt tea gea ttt tgt eet tat tgg aca ata gea agg
                                                                       164
Ser Glu Val Gln Phe Ser Ala Phe Cys Pro Tyr Trp Thr Ile Ala Arg
            -55
                                 -50
                                                                       212
ata tta gaa cgt gtt ggt tcc gcg tgc ttc cgt ctt gag tta tgt gct
Ile Leu Glu Arg Val Gly Ser Ala Cys Phe Arg Leu Glu Leu Cys Ala
        -40
                             -35
                                                 -30
get att gtc gga tat ttt gtc tta gat gta cgt act ttc ctg ttc att
                                                                       260
Ala Ile Val Gly Tyr Phe Val Leu Asp Val Arg Thr Phe Leu Phe Ile
                         -20
gtg gta tgt gta att tgc gtt act ttg aat ttt cca cgt ttt tac ttt
                                                                       308
```

25 gcggtgaagc tttcccattt tatgtgcaga ttattttcag agggtatata gaattcaggc agctgtttcg ttgtagcaca ttaaaaatat tttcccactt caaaaaaaaa aaacc

1

356

411

471

526

Val Val Cys Val Ile Cys Val Thr Leu Asn Phe Pro Arg Phe Tyr Phe

ctt tgt ctc tca tca ctt acc gct ttt ggg acc ccc ccc atc ggg gtt

Leu Cys Leu Ser Ser Leu Thr Ala Phe Gly Thr Pro Pro Ile Gly Val

cac att ccc tct ccc tararcacac tcccttggat ttcctcradt ggggtctgct

-5

-10

His Ile Pro Ser Pro

<210:	> 32	0														
<211:	> 98	9														
<212:	> DN.	A														
<213:	> Ho	mo s	apie	ns												
<220:		0														
<221:			i								•					
<222	> 44	81	4 ',				,	,								
<221				е				•								,
<222							•									
<223						2406										•
			LLLX			3486 LE						•				•
<221	-		•													
<222	> 91	89	,					1	•							
<400 aaat			cacc	cado	t to	etac	ctat	tac	tctc	αас	agt	ato	cga	aga	ata	· 55
aaac	9-9-	ac a	egee	cage		.0090	cogo							Arg	Ile	
															-20	
tcc	ctg	act	tct	agc	cct	gtg	cgc	ctt	ctt	ttg	tdt	ctg	ctg	ttg	cta	103
Ser				-15					-10					-5		
cta	ata	gcc	ttg.	gag	atc	atg	gtt	ggt	ggt	cac	tct	cţt	tgc	ttc	aac	151
Leu	Ile	Āla	Leu 1	Glu	Ile	Met	Val 5	Gly	Gly	His	Ser	Leu 10	Cys	Phe	Asn	
ttc	act	ata		tica	tta	tcc	_	cct	qqa	caq	ccc		tgt	gaa	gcg	199
Phe	Thr	Ile	Lvs	Ser	Leu	Ser	Arq	Pro	Gly	Gln	Pro	Trp	Cys	Glu	Ala	
	15		_,,			20	5				25	•	•			
		ttc	tta	aat	aaa	aat	ctt	ttc	ctt	cag	tac	aac	agt	gac	aac	247
His	Val	Phe	Leu	Asn	Lys	Asn	Leu	Phe	Leu	Gln	Tyr	Asn	Ser	Asp	Asn	
30					35					40	_				45	
aac	atg	qtc	aaa	cct	ctg	ggc	ctc	ctg	999	aag	aag	gta	tat	gcc	acc	295
Asn	Met	Val	Lys	Pro	Leu	Gly	Leu	Leu	Gly	Lys	Lys	Val	Tyr	Ala	Thr	
				50					55					60		
agc	act	tgg	gga	gaa	ttg	acc	caa	acg	ctg	gga	gaa	gtg	ggg	cga	gac	343
Ser	Thr	Trp	Gly 65	Glu	Leu	Thr	Gln	Thr 70	Leu	Gly	Glu	Val	Gly 75	Arg	Asp	
ctc	200	2+0		ctt	tat	gac	atc		ccc	car	ata	aaq		aαt	gat	393
Len	Arg	Met	T.em	Leu	Cve	Asp	Tle	Lvs	Pro	Gln	Tle	Lvs	Thr	Ser	Asp	
Deu	nr 9	80	Deu	Deu	<b>C</b> 10	p	85	-, -				90			-	
cct	tcc		cta	caa	atc	kar		ttt	tqt	caa	cqt	gaa	gca	gaa	cgg	439
Pro	Ser	Thr	Leu	Gln	Val	Xaa	Xaa	Phe	Cys	Gln	Arg	Glu	Ala	Glu	Arg	
	95					100			-		105					
tgc		ggt	qca	tcc	tgg	cag	ttc	gcc	acc	aat	gga	gag	aaa	tcc	ctc	48
Cys	Thr	Gly	Āla	Ser	Trp	Gln	Phe	Ala	Thr	Asn	Gly	Glu	Lys	Ser	Leu	
110		•			115					120					125	
ctc	ttt	gac	gca	atg	aac	atg	acc	tgg	aca	gta	att	aat	cat	gaa	gcc	53
Leu	Phe	Asp	Ala	Met	Asn	Met	Thr	Trp	Thr	Val	Ile	Asn	His	Glu	Ala	
				130					135					140		
agt	wag	atc	aag	gag	aca	tgg	aag	aaa	gac	aga	ngg	ctg	gaa	aak	tat	58
Ser	Xaa	Ile	Lys	Glu	Thr	Trp	Lys	Lys	Asp	Arg	Xaa	Leu	Glu	Xaa	Tyr	
			145					150					155		<b>-</b>	
ttc	agg	aag	ctc	tca	aar	gga	gac	tgc	gat	cac	tgg	ctc	agg	gaa	ひとっ	63
Phe	Arg		Leu	Ser	Lys	Gly		Cys	Asp	His	Trp		Arg	GIU	Fue	
		160					165	<b></b> -				170		~	22+	67
tta	999	cac	tgg	gaa	gca	atg	cca	rad	ccg	ama	gtg	cem	cca	rtd	aat	0 /

Leu Gly His Trp Glu Ala Met Pro Xaa Pro Xaa Val Ser Pro Xaa Asn 175 180 185	
get tea raw ate eac tgg tet tet tet art eta eca raw ara tgg ate	727
	,
Ala Ser Xaa Ile His Trp Ser Ser Ser Xaa Leu Pro Xaa Xaa Trp Ile	
190 195 200 205	
atc ctg ggg gca ttc atc ctg tta vtt tta atg gga att gtt ctc atc	775
Ile Leu Gly Ala Phe Ile Leu Leu Xaa Leu Met Gly Ile Val Leu Ile	
· · · · · · · · · · · · · · · · · · ·	
tgt gtc tgg tgg caa aat ggc ara ara tcc acc tad arg tgataccacg	824
Cys Val Trp Trp Gln Asn Gly Xaa Xaa Ser Thr Xaa Xaa	
225 230	
	884
geggegeaaa attgtteace tgtggteete gategetgae ageettgget eccaetgetg	
tgtgttccct gagtcaagtg gaggcggagc ctgcaatgag cggaratcgc gcctctgcat	944
tccagtcttg gcaacagarc aagactccgt ctcaaaaaaa aaaaa	989
·	
	·
· · · · · · · · · · · · · · · · · · ·	
<210> 321	
<211> 1017	
<212> DNA	
· · · · · · · · · · · · · · · · · · ·	
<213> Homo sapiens	
<220>	•
<221> CDS	
<222> 3581	
<221> sig_peptide	
<222> 3182	
· · · · · · · · · · · · · · · · · · ·	
<223> Von Heijne matrix	
score 6.69999980926514	
seg LWPFLTWINPALS/IC	
seq LWPFLTWINPALS/IC	
•	
<221> polyA_site	
•	
<221> polyA_site	
<221> polyA_site <222> 10061016	
<221> polyA_site <222> 10061016 <400> 321	47
<221> polyA_site <222> 10061016  <400> 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg	47
<221> polyA_site <222> 10061016 <400> 321	47
<221> polyA_site <222> 10061016  <400> 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg	47
<221> polyA_site <222> 10061016  <400> 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu -60 -55 -50	<b>4</b> 7 95
<221> polyA_site <222> 10061016  <400> 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60	
<221> polyA_site <222> 10061016  <400> 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60	
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu   -60</pre>	95
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu   -60</pre>	95 143
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu         -60</pre>	95 143 191
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg   Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu         -60</pre>	95 143 191
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191 239
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191 239
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191 239 287
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191 239
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191 239 287
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191 239 287
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg     Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287 335
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg     Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287 335
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287 335
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg     Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu</pre>	95 143 191 239 287 335 383
<pre>&lt;221&gt; polyA_site &lt;222&gt; 10061016  &lt;400&gt; 321 ac atg tgc cct agt ctg gaa gag gct ccc agt gtc aag ggg act ctg    Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu    -60</pre>	95 143 191 239 287 335

70 75 80 ttc cas aaa cat ctg ttg gtg ctg ctg gtg gct gtg gcc cat agt gtt	479
Phe Xaa Lys His Leu Leu Val Leu Leu Val Ala Val Ala His Ser Val	
85 90 95 ctg gaa cca cct gcc ctg gtc cca aat gtg cag tgt gag atg tgc aca	527
Leu Glu Pro Pro Ala Leu Val Pro Asn Val Gln Cys Glu Met Cys Thr	
100 105 110 . 115	
cac tca ggg ccc cgt gac ctg gaa gcc gca gtc gtg tcc cca gca cct	575
His Ser Gly Pro Arg Asp Leu Glu Ala Ala Val Val Ser Pro Ala Pro	•
tgg gaa tgagcctgtc ctctgtgtga aggagggggt ggttctcaaa ccactgactc	631
Trp Glu ttggtgctca ggaggggcct gctgctgtcc tgggcatggg gtggtcattg ttcaagactg	691
aggcagacte agtettigaa agggtgeaga ggceaggege ggtggeteae geetgtaatt	751
ccagcacttt gggaggccaa ggtggacaga tcatgaggtc aggagttcga gaccagcctg	811
gccaatacgg tgaaaccgca tctctactaa rraatawcaw aaattagtcg ggcatgggtg	871 · 931
atgtgtgctt gtagtcccag ctactcatga ggyctgaggc agaagaatca cctgaatctg	991
ggaggcagag gttgcagtga accaagatcg cacgactgta caccagcctg ggcgacagag	1017
tgagactccg tctcaaaaaa aaaaam	
<210> 322	
<211> 529	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 107427	
<221> sig_peptide	
<222> 107190	
<223> Von Heijne matrix score 3.7999995231628	
seq RFLSLSAADGSDG/SH	
beg Middub.abebbe, es	
<221> polyA_signal	
<222> 499504	•
<221> polyA_site	
<222> 516529	
<400> 322	
aaagtcagcg ctggagtcgg ctaggcggct ggaaacggcg gctgccgccg gtgactcagg	60
gaggeggag geegmsqqmq gagetettee tgeaggegtg garace atg gtg ete	115
Met Val Leu	1.63
acg ctc gga gaa agt tgg ccg gta ttg gtg ggg agg agg ttt ctc agt	163
Thr Leu Gly Glu Ser Trp Pro Val Leu Val Gly Arg Arg Phe Leu Ser	
-25 -20 -15 -10 ctg tee gea gee gae gge age gat gge age cae gae age tgg gae gtg	211
Leu Ser Ala Ala Asp Gly Ser Asp Gly Ser His Asp Ser Trp Asp Val	
-5 1 5	
gag ege gte gee gag tgg eee tgg ete tee ggg ace att ega get gtt	259
Glu Arg Val Ala Glu Trp Pro Trp Leu Ser Gly Thr Ile Arg Ala Val	
10 15 20	200
tcc cac acc gac gtt acc aag aag gat ctg aag gtg tgt gtg gaa ttt	307
Ser His Thr Asp Val Thr Lys Lys Asp Leu Lys Val Cys Val Glu Phe	
25 30 35 gak ggg gaa tot tgg agg aaa aga aga tgg ata gaa gto tac ago ott	355
Xaa Gly Glu Ser Trp Arg Lys Arg Arg Trp Ile Glu Val Tyr Ser Leu	
40 45 50 55	

cta agg aaa gca ttt tta gta aaa cat aat ttg gtt tta gct gaa cga Leu Arg Lys Ala Phe Leu Val Lys His Asn Leu Val Leu Ala Glu Arg 60 65 70	403
aag tca cct gaa att tct tgg ggt taaccatctt tagttaaatg gaattttaat Lys Ser Pro Glu Ile Ser Trp Gly 75	457
ttaaatgacg ctttgctaat tttaagtgtt aagcattttg cattaaaata ttcatataat aaaaaaaaaa	517 529
<210> 323	
<211> 1046	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS <222> 45407	•
<pre>&lt;221&gt; sig_peptide &lt;222&gt; 4583</pre>	
<223> Von Heijne matrix	
score 5.69999980926514 seg MLVLRSALTRALA/SR	
-	
<221> polyA_signal	•
<221> polyA_site <222> 10321042	
<400> 323	
aaaaggacac ggctggctgc ttttctcagc gccgaagccg cgcc atg ctc gtc ctc  Met Leu Val Leu -10	56
aga age gee etg act egg geg etg gee tea egg acg etg geg eet eag	104
Arg Ser Ala Leu Thr Arg Ala Leu Ala Ser Arg Thr Leu Ala Pro Gln -5 1 5	•
atg tgc tca tct ttt gct acg gga ccc aga caa tac gat gga ata ttc	152
Met Cys Ser Ser Phe Ala Thr Gly Pro Arg Gln Tyr Asp Gly Ile Phe 10 15 20	
tat gaa ttt cgt tct tat tac ctt aag ccc tca aag atg aat gag ttc	200
Tyr Glu Phe Arg Ser Tyr Tyr Leu Lys Pro Ser Lys Met Asn Glu Phe 25 30 35	
ctg gaa aat ttt gag aaa aac gct caa ctt cgg aca gct cac tct gaa	248
Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr Ala His Ser Glu	
40 45 50 55 ttg gtt gga tac tgg agt gta kaa ttt gga ggc aga atg awt aca gtg	296
Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg Met Xaa Thr Val	
60 65 70 ttt cat att tgg aag tat gat aat ttt gct cat cga act gaa ttt cag	344
Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg Thr Glu Phe Gln	
75 80 85	392
aaa gcc ttg gcc aaa gat aag gaa tgg caa gaa caa ttc ctc att cca Lys Ala Leu Ala Lys Asp Lys Glu Trp Gln Glu Gln Phe Leu Ile Pro	ے ر ر
90 95 100	4.47
aat ttg gct ctc aat tgataaacaa gatagtgaga ttacttatct ggtaccatgg Asn Leu Ala Leu Asn	447
105	E 0.0
tgcaaattag aaaaacctcc aaaagaagga gtctatgaac tggccacttt tcagatgaaa cctggtgggc cagctctgtg gggtgatgca tttaaaaggg cagttcatgc tcatgtcaat	507 567
	•

627

802

862

880

ctaggctaca caaaactagt tggagtgttc cacacagagt acggagcact caacagagtt

```
catgttcttt ggtggaatga gagtgcagat agtcgtgcag ctgggagaca taagtcccat
                                                                    687
gaggatccca gagttgtggc agctgttcgg gaaagtgtca actacctagt atctcagcag
                                                                   747
aatatgette tgatteetae ategttttea ceaetgaaat agttttetae tgaaatacaa
                                                                    807
aacatttcat taactgctat aggatctgtc tgctaatggt gcttaaattc tcccaagagg
                                                                    867
ttctcacttt tatttgaagg aggtggtaag ttaatttgct atgtttcttg cattatgaag
                                                                   927
gctacatctg tgctttgtaa gtaccacttc aaaaaatakt tctgtttact ttctgcatgg
                                                                   987
tatttcagtg tctgtcatac attaaaaata cttgtcactg tttyaaaaaa aaaaammcc
                                                                  1046
<210> 324
<211> 880
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 201..332
<221> sig_peptide
<222> 201..251
<223> Von Heijne matrix
     score 7.80000019073486
     seq VLWLISFFTFTDG/HG
<221> polyA site
<222> 869..880
<400> 324
aattgctgat ggatcagtga gcctgtgttc atgccagtga gctgctgtgg ctcagatact
                                                                    60
gatactttct ttccaaacag cataagaagt gattgancca caagtatact gaaggmargg
                                                                   120
yhoccwsvar tyctggwgtg amgagataaa tcaccagtca cagactatgc acccgactgc
                                                                   180
tgctgttcag tccagggaaa atg aaa gtt gga gtg ctg tgg ctc att tct ttc
                                                                   233
                     Met Lys Val Gly Val Leu Trp Leu Ile Ser Phe
                             -15
                                                                   281
tte ace tte act gae gge cae ggt gge tte etg ggg gtg agt tgg tge
Phe Thr Phe Thr Asp Gly His Gly Gly Phe Leu Gly Val Ser Trp Cys
    -5
329
Tyr Val Ser Tyr Leu Phe Ser Thr Asn Ser Pro Leu Ser Phe Arg Arg
                                   20
att tagaacccct cactctctag gggactgcaa ctgcataatt taatgtactt
                                                                   382
gagatcagaa gtcctgagtt ctcgtttcaa cattaccaac attcactgtg tggccttgga
                                                                    442
taagtragtc atttcatctc ttcggagctt agatgatcma actgcaarag gaggatcttt
                                                                   502
                                                                    562
gattamacta tottagagat cttttccagt tcaacacatg ctgtactatg gcttctcgga
tgcagaaaaa tcacatggat ggacattagc aatccttara cactgtcttt cctgtctaca
                                                                    622
ctcgcttgag tgatgckttc atctaggatc atggttttaa tattctctac atgctgatga
                                                                    682
ctcccagctg tatagctcca tctcagaacc tctcccctgt ccacactcac atatccatta
                                                                    742
```

cctacgtgtt atttccagct gggaaatcca gcggaacctc ggnaacttca tttgnttcaa

aatcgnaacc caatcettet tgeetatete ageaagtggt atcactatet ttecagetae

<210> 325

<211> 1217

<212> DNA

<213> Homo sapiens

ttaggcaaaa aaaaaaaa

<221> CDS <222> 217..543 ' <221> sig\_peptide <222> 217..255 <223> Von Heijne matrix score 6.40000009536743 seq MCLLTALVTQVIS/LR <221> polyA site <222> 1206..1217 <400> 325 aatgccagtg tcagcttctc tccgaaaact gggtaatacg aaatggtctt tattggttgt gaacactcga gctgagaaac attttaggat ctttgtgtct tttgtgatga ttttgtttct 120 graagrwgga aasctgtcta aaaatattca agtgtgcaac caaggattta gatgaagcca 180 234 gcaaacaaag gaatcatgta atcaggacct gagcga atg tgc tta ctc acg gcg Met Cys Leu Leu Thr Ala -10 282 tta gtt aca cag gtg att tcc tta aga aaa aat gca gag aga act tgt Leu Val Thr Gln Val Ile Ser Leu Arg Lys Asn Ala Glu Arg Thr Cys tta tgc aag agg aga tgg ccc tgg ngc ccc tcg ccc cgg atc tac tgc 330 Leu Cys Lys Arg Arg Trp Pro Trp Xaa Pro Ser Pro Arg Ile Tyr Cys 20 15 378 tca tcc acc cca tgc gat tcc aaa ttc ccc acc gtc tac tcc agt gcc Ser Ser Thr Pro Cys Asp Ser Lys Phe Pro Thr Val Tyr Ser Ser Ala 426 cca ttc cat gcc ccc ctc ccc gtc cag aat tcc tta tgg ggg cac ccg Pro Phe His Ala Pro Leu Pro Val Gln Asn Ser Leu Trp Gly His Pro 45 50 474 ctc cat ggt tgt tcc tgg caa tgc cac cat ccc cag gga car aat ctc Leu His Gly Cys Ser Trp Gln Cys His His Pro Gln Gly Gln Asn Leu 65 cag cct gcc agt ctc cad acc cat ctc tcc aag ccc aag cgc cat ttt 522 Gln Pro Ala Ser Leu Xaa Thr His Leu Ser Lys Pro Lys Arg His Phe 573 ara aar aar rra tgt caa gcc tgatgaarac atgagtggca aaaacattgc Xaa Lys Lys Xaa Cys Gln Ala aatgtacara aatgagggtt tctatgctga tccttacctt tatcacgagg gacggatgag 633 catascetea teccatggtg gacacecaet ggatgteece gaccacatea ttgcatatea 693 ccgcaccgcc atccggtcag cgagtgctta ttgtaacccc tcaatgcaag cggaaatgca 753 tatggaacaa tcactgtaca gacagaaatc aaggaaatat ccggatagcc atttgcctac 813 873 actgggctcc aaaacacccc ctgcctctcc tcacagaktc agtgacctga ggatgataga 933 catgcacgct cactataatg cccacggccc ccctcacacc atgcagccag accgggcctc teegageege caggeettta aaaaggagee aggeacettg gtgtatatag aaaageeacg 993 gagegetgea ggattateca geettgtaga eeteggeeet eetetaatgg agaageaagt 1053 ttttgcctac agcacggcga caatacccaa agacagagag accagagaga ggatgcaagc 1113 catggagaaa cagattgcca gtttaactgg ccttgttcag tctgcgcttt ttaaagggcc 1173 cattacaagt tatagcaaar atgcgtctag ctaaaaaaaa aaaa 1217

<sup>&</sup>lt;210> 326

<sup>&</sup>lt;211> 959

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;220>

<sup>&</sup>lt;221> CDS

<sup>&</sup>lt;222> 18..446

```
<221> sig peptide
 <222> 18..140
 <223> Von Heijne matrix
       score 4.09999990463257
       seg GILILWIIRLLFS/KT
 <221> polyA_signal
  <222> 930..935
  <221> polyA_site
  <222> 948..959
' ₹400> 326
                                                                       50
  aaaggaagcg gctaact atg gcg acc gcc acg gag cag tgg gtt ctg gtg
                    Met Ala Thr Ala Thr Glu Gln Trp Val Leu Val
                                            -35
  gag atg gta cag gcg ctt tac gag gct cct gct tac cat ctt att ttg
                                                                       98
  Glu Met Val Gln Ala Leu Tyr Glu Ala Pro Ala Tyr His Leu Ile Leu
                     -25
                                         -20
  gaa ggg att ctg atc ctc tgg ata atc aga ctt ctt ttc tct aag act
                                                                      146
  Glu Gly Ile Leu Ile Leu Trp Ile Ile Arg Leu Leu Phe Ser Lys Thr
                 -10
                                     -5
                                                                      194
  tac aaa tta caa gaa cga tct gat ctt aca gtc aag gaa aaa gaa gaa
  Tyr Lys Leu Gln Glu Arg Ser Asp Leu Thr Val Lys Glu Lys Glu Glu
                             10
  ctg att gaa gag tgg caa cca gaa cct ctt gtt cct cct gtc cca aaa
                                                                      242
  Leu Ile Glu Glu Trp Gln Pro Glu Pro Leu Val Pro Pro Val Pro Lys
                         25
                                                                      290
  gac cat cct gct ctc aac tac aac atc gtt tca ggc cct cca agc cac
  Asp His Pro Ala Leu Asn Tyr Asn Ile Val Ser Gly Pro Pro Ser His
                      40
                                         45
                                                                      338
  aaa act gtg gtg aat gga aaa gaa tgt ata aac ttc gcc tca ttt aat
  Lys Thr Val Val Asn Gly Lys Glu Cys Ile Asn Phe Ala Ser Phe Asn
                  55
                                     60
                                                                      386
  ttt ctt gga ttg ttg gat aac cct agg gtt aag gca gca gct tta gca
  Phe Leu Gly Leu Leu Asp Asn Pro Arg Val Lys Ala Ala Ala Leu Ala
                                 75
                                                                      434
  tct cta aag aag tat ggc gtg ggg act tgt gga ccc tgt gga ttt tat
  Ser Leu Lys Lys Tyr Gly Val Gly Thr Cys Gly Pro Cys Gly Phe Tyr
                              90
                                                                      486
  ggc aca ttt gaa tgaaratgaa ggatcattga tttccttgtg tatggataat
  Gly Thr Phe Glu
      100
  ccgggaacag gccaactaaa tatttgatga atgtatgatt tcaaatacag tgaattccct
                                                                      546
  gggagtcatc aaaraagacg gcattttatg gttgttttta ttaagtgtat attctttgct
                                                                      606
                                                                      666
  cctgaaaatg ttattaaata attgtttagg ccgggcatgg tggctcatgc ctgtaatccc
  agcactttca aaggotgagg caggoagatc acctgaggtc aggagttcaa aaccagcctg
                                                                      726
  gccaacatgc tgaaacctcg tctctactaa aaatacaaaa attagctggg cgtggtggtg
                                                                      786
  grtgcctgtg gtcccagctr cgtgggaggc tgaggtggga gaattgcttc aacctgggag
                                                                      846
  geggaggttg cagtgageeg agateatgee actgeactee ageetgggea acagageaag
                                                                      906
  959
```

<210> 327

<211> 921

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 29..724 " <221> sig\_peptide <222> 29..118 <223> Von Heijne matrix score 3.90000009536743 seg VAHALSLPAESYG/NX <221> polyA\_signal <222> 886..891 <221> polyA site <222> 910..920 <400> 327 aaggagccac gctttcgggg gttgcaag atg gcg gcc acc agt gga act gat 52 Met Ala Ala Thr Ser Gly Thr Asp -25 -30 100 gag ccg gtt tcc ggg gag ttg gtg tct gtg gca cat gcg ctt tct ctc Glu Pro Val Ser Gly Glu Leu Val Ser Val Ala His Ala Leu Ser Leu -15 cca gca gag tcg tat ggy aac grt yct gac att gag atg gct tgg gcc 148 Pro Ala Glu Ser Tyr Gly Asn Xaa Xaa Asp Ile Glu Met Ala Trp Ala atg aga gca atg cag cat gct gaa gtc tat tac aag ctg att tca tca 196 Met Arg Ala Met Gln His Ala Glu Val Tyr Tyr Lys Leu Ile Ser Ser 20 15 244 gtt gac cca cag ttc ctg aaa ctc acc aaa gta gat gac caa att tac Val Asp Pro Gln Phe Leu Lys Leu Thr Lys Val Asp Asp Gln Ile Tyr 35 tct gag ttc cgg aaa aat ttt gag acc ctt agg ata gat gtg ttg grc 292 Ser Glu Phe Arg Lys Asn Phe Glu Thr Leu Arg Ile Asp Val Leu Xaa 45 cca gaa gan ctc aag tca gaa tca gcn aaa gag ccc cca gga tac aat 340 Pro Glu Xaa Leu Lys Ser Glu Ser Ala Lys Glu Pro Pro Gly Tyr Asn 388 tct ttg cca ttg aaa ttg ctc gga acc ggg aag gct ata aca aag ctg Ser Leu Pro Leu Lys Leu Leu Gly Thr Gly Lys Ala Ile Thr Lys Leu 75 80 ttt ata tca gtg ttc agg aca aag gag aga aag gag tca aca atg 436 Phe Ile Ser Val Phe Arg Thr Lys Lys Glu Arg Lys Glu Ser Thr Met 100 gag gag aaa aaa gag ctg aca gtg gag aag aag aga aca cca aga atg 484 Glu Glu Lys Lys Glu Leu Thr Val Glu Lys Lys Arg Thr Pro Arg Met 115 110 532 gag gag aga aag gag ctg ata gtg gag aag aaa aag agg aag gaa tca Glu Glu Arg Lys Glu Leu Ile Val Glu Lys Lys Lys Arg Lys Glu Ser 125 130 580 aca gag aag aca aaa ctg aca aag gag gag aaa aag gga aag ctg Thr Glu Lys Thr Lys Leu Thr Lys Glu Glu Lys Lys Gly Lys Leu 145 628 aca aag aaa tca aca aaa gtg gtg aaa aag cta tgt aag gta tac agg Thr Lys Lys Ser Thr Lys Val Val Lys Lys Leu Cys Lys Val Tyr Arg gaa cag cac tot aga ago tat gac toa att gag act aca agt acc acg 676 Glu Gln His Ser Arg Ser Tyr Asp Ser Ile Glu Thr Thr Ser Thr Thr 180 gtg cta ctt gca cag acc cct ttg gtt aaa tgt aaa ttc ttg tac aat 724 Val Leu Leu Ala Gln Thr Pro Leu Val Lys Cys Lys Phe Leu Tyr Asn 190

tgaaggatac gcagaaggac atctttctag tctaacagtc aggagetgct ctggtcattc ccttgtatga actggtctaa agactgttag tggggtgtta gttgatttt cctggtatac

784

844

tgtttcttgg ctgacactac tggtcaagta agaaatttgt aaataaattt cttttggttc 904 921 ttattaamaa aaaaaas <210> 328 <211> 1344 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 404..586 <221> sig\_peptide <222> 404..466 <223> Von Heijne matrix score 4.09999990463257 seq SLMFFSMMATCTS/NV <221> polyA signal <222> 1304..1309 <221> polyA site <222> 1334..1344 <400> 328 60 ataatttaat gcaaaatatc cttttatgaa tttcatgtta atattgtgaa atattaaaat 120 aattccacaa tagttgagaa aaatgagcat ttttttccat ttttaaaaaaa tgcatagaaa agacaatttt aaaatcctgg gamccawatt tatttagaag tagctgttag taaaacatta 180 240 gaaaaggagt caggccatba ggttatttat nbnaatctct aagcaattag gntgaagtta 300 ttaagtcaag cctagaaaag ctgcctcctt gtaaggcttt catgacaatg tatagtaatc breagtgtcc aattettege acteetcagg aatateacta cetcaggtta eggtacacag 360 415 gctataattg atgatgatgt tcagataact gaagacacaa taa atg aca ttc aga Met Thr Phe Arg cat cag gac aat too oto atg tto ttt tot atg atg goo acc tgt acc 463 His Gln Asp Asn Ser Leu Met Phe Phe Ser Met Met Ala Thr Cys Thr -15 -10 age aac gtg ggt tte ace cae aca acg atg aac tgt tet ett act tet 511 Ser Asn Val Gly Phe Thr His Thr Thr Met Asn Cys Ser Leu Thr Ser 10 559 cca gtt gat ttt aaa gac ttg tta aga gtc tta cta ata aaa ttt ggg Pro Val Asp Phe Lys Asp Leu Leu Arg Val Leu Leu Ile Lys Phe Gly 25 20 606 tat gat aga aaa tcc aca atc aaa tct tgaaccaaat aacatattaa Tyr Asp Arg Lys Ser Thr Ile Lys Ser 35 666 attactaata tttaaqtqat qqaaqacaca caaaaaactt aaaagcacga acaacctaac 726 ttgaaaaara attttaaaat atgattaacc tgaaraaaar araatcctaa ragccaaagc tcctttttat ttagcttgga attttcctat tggttcctaa caaactgtcc caatgtcata 786 846 taaggaaaca tgatctatta cattccttta taacaacgtg gararactat aaacctatgt 906 aagtagtaaa actatatcag adactcagga ractgactww aaggcctgga tctgcagtgt 966 attatctqta taaaaattqq cagggggaag ctaaaaggaa aqqagattgg agatctcaat totatcatgg tqtatttcat acgcaaatca ragcatgcat tgttttttgt ttttggaaar 1026 avaarggaag tgtgttctgc cccatgtttc cttccgtgtt tatagttcaa actctatata 1086 1146 tacttcaggt attttttgtt tagcccttca ttataaatgg gcaggaaatt gtttatcaac 1206 ctagccagtt tattactagt gaccttgact tcagtatctt gagcattctt ttatattttt 1266 cttttattat cctqaqtctq taactaaaca attttgtctt caaattttta tccaatatcc attgcaccac accaaatcaa gcttcttgat tttcaaaaaat aaaaaggggg aaatacttac 1326 1344

aacttgtaaa aaaaaaa

```
<210> 329
<211> 585
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 331..432
<221> sig_peptide
<222> 331..387
<223> Von Heijne matrix
      score 7
      seq AGLSSCLLPLCWL/ER
<221> polyA_signal
<222> 548..553
<221> polyA site
<222> 573..585
<400> 329
                                                                       60
aagcctaggt gtggcgccc gaccggactt tcacttctgg ccagcccttt ccccacctgg
gcgcgggass ggtgccagtc tttaaacaac ctctcgatgg gtcccacgaa gatgtttcca
                                                                      120
gaccettgga atgccaagtt caagtttage tatgtetege ggagaggeeg gtggaagaag
                                                                      180
caacgagaat gaagcacccc agttctctgc tgagcacatg ggcatctgca ataaagattt
                                                                      2.40
                                                                      300
aatttcccag cttctcctga agctcggtat ggccacaaca ctaaattctg cccgaggaga
ttgagcaaaa tagtatggga cttccaagaa atg ttt tta aag tca ggg gca ggc
                                                                      354
                                 Met Phe Leu Lys Ser Gly Ala Gly
ctt tct tca tgc ctt ctt cct ctt tgc tgg ctg gaa cgc aaa gac cat
                                                                      402
Leu Ser Ser Cys Leu Leu Pro Leu Cys Trp Leu Glu Arg Lys Asp His
    -10
                         -5
                                                                      452
ggc agg agg cca agc asc cat cct gga agg tgaaagcctc atactaagga
Gly Arg Arg Pro Ser Xaa His Pro Gly Arg
                10
cgtcaracag cgaaataara rcctgggtcc ttgaccctgt aaasatctcc ctccccatcc
                                                                      512
tggtctgtct gccttgactc ctttcatatg aaaaaaataa acttttaact tgcgtwaacc
                                                                      572
                                                                      585
aaaaaaaaa aaa
<210> 330
<211> 914
```

<221> polyA\_site <222> 903..914

<400> 330 acaaatatca atgatgttta tgaatctagt gtgaaagtkt taatcacatc acaaggct	58
atg aac rra tat gca agt cca ttc aac tgw caa ttg ard tat ttg gak	106
Met Asn Xaa Tyr Ala Ser Pro Phe Asn Xaa Gln Leu Xaa Tyr Leu Xaa	
-50 -45 -40	
ttg agc agr ttc gag tgt gtr cat aga gat gga aga gta att aca ctg	154
Leu Ser Arg Phe Glu Cys Val His Arg Asp Gly Arg Val He Thr Leu	
-35 -30 ** <sup>25</sup>	202
tet tat cag gag cag gag cta cag gat ttt ett etg tet cag atg tea	202
Ser Tyr Gln Glu Gln Leu Gln Asp Phe Leu Leu Ser Gln Met Ser	
-20 -15 -10 -10 are are are are are	250
cag cac cag gta cat gca gtt cag caa ctc gcc aag gtt atg ggc tgg	
Gln His Gln Val His Ala Val Gln Gln Leu Ala Lys Val Met Gly Trp  10	
-5 caa gta ctg agc ttc agt aat cat gtg gga ctt gga cct ata gag agc	298
Gln Val Leu Ser Phe Ser Asn His Val Gly Leu Gly Pro Ile Glu Ser	
15 20 25	
abt ggt aat gca tot gcc atc acg gtg gcc ccc caa gtg gtg act atg	346
Xaa Gly Asn Ala Ser Ala Ile Thr Val Ala Pro Gln Val Val Thr Met	
30 35 40	
cta ttt cag ttc gta atg gac ctg aaa gtg gca gca aga tta tgg ttc	394
Leu Phe Gln Phe Val Met Asp Leu Lys Val Ala Ala Arg Leu Trp Phe	
45 50 55	442
agt ttc ctc gta acc aat gta aar acc ttc caa aaa gtg atg ttt tac	442
Ser Phe Leu Val Thr Asn Val Lys Thr Phe Gin Lys Val Met Phe lyr	
60 65 70	490
aar ata aca aat gga gtc atc ttc gtg ggc cat tca aar aag ttc agt	
Lys Ile Thr Asn Gly Val Ile Phe Val Gly His Ser Lys Lys Phe Ser	
gga ata aaa tgg aag gtc kaa att ttg ttt ata aaa tgg arm tgc tta	538
Gly Ile Lys Trp Lys Val Xaa Ile Leu Phe Ile Lys Trp Xaa Cys Leu	
gry rie bys rip bys var kaa rie bed rie 110 170 170 170 170 170 170 170 170 170	
tgt ctg cac tta gcc ctt gtc tac tat gat ttt ttc car atg ttt cct	586
Cys Leu His Leu Ala Leu Val Tyr Tyr Asp Phe Phe Gln Met Phe Pro	
110 115 120	
aga rag off too are ago tit gao tig aga tgt tig car ato ago tat	634
Lys Xaa Val Ser Xaa Asn Phe Asp Leu Lys Cys Leu Gln Ile Asn Tyr	
125 130 135	600
aag cac aaa gaa gar ata act tcc aaa aga gtg ctg ttt tta aaa ata	682
Lys His Lys Glu Glu Ile Thr Ser Lys Arg Val Leu Phe Leu Lys IIe	
140 145 150	733
ata att agg aaa tgt ttt att tagcactttc aaacttttca ctttataaat	,,,,
Ile Ile Arg Lys Cys Phe Ile	
155 160	793
gacaagtgct ttgaaatgca gaagtttatg tacagttgta tatacagtat gacaagatgt	853
aaaataatat gtttttcatg cagtttaaaa tattactaac ttaagggttt ctatgtgctt	913
tttaaaatat tccttctttg atgttgacat caaataaagt atgtggttta aaaaaaaaaa	914
a	

<210> 331

<211> 1161

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 672..752

WO 99/31236 -248- PCT/IB98/02122 -

```
<221> sig peptide
<222> 672..722
<223> Von Heijne matrix
     score 4.30000019073486
     seg LLYAHLSFTSKRA/VV
<221> polyA site
<222> 1150..1161 -
<400> 331
                                                                       60
aagatatcac tgtcttgttt tcacttagat cctacttaca aagtgagggt tattaacaga
ataaagcctt cctttaaagc tttataataa tcatatttat taataatgct gttgtgcata
                                                                      120
cttatagtat gcatatattc agcatatgtt gcatgtsttc agaattacat aagatgaaat
                                                                      240
ccctttcatt gcaacttgca agtgagaaaa gatccttagt ggctctggtg gaagaaatag
tatttcttct tctcagggtg tctccctgcc ttggcccctc ccagaagccc cggctttaaa
                                                                      300
agtgaaaatg tttgaaacat gaaacatgtc tgtaggaagc atcagcatgg ccataagtgc
                                                                      360
                                                                      420
artgattttc atatatgcct ctgcccattt caaatatatt tttgacatga ataaatctaa
cagtatacar aataattcat gtaaraccct aacgtgtaca tgtgaaaaag catttctata
                                                                      480
taatgtgagg agcactggcc atcaattagg gaaataaagg tcatgtaata ttgcaaattt
                                                                      540
                                                                      600
tcaaaataga gcsstgcaag ataactgcaa tcataccaaa aactatttga gtaaatggat
ttttaaagta attttgttt aaaaaaattt atatttcaga agsagaaaat gtcaaatgat
                                                                      660
-agtotttgta a atg gtg gtg cac ott oto tat goa cat otg tot ttt aca
                                                                      710
             Met Val Val His Leu Leu Tyr Ala His Leu Ser Phe Thr
                                         -10
                     -15
                                                                      752
tca aaa aga gct gtg gtc atg cta aaa tta gag ata act ttt
Ser Lys Arg Ala Val Val Met Leu Lys Leu Glu Ile Thr Phe
tgaatgactt ggtcaagctg tgtgtaaaat atttaaccat aagtcaagta cagtgtacta
                                                                      812
tgtttaataa agttacattt aatgcattta ttgcatatat gaatatatac atgaagaggc
                                                                      872
tttatgtctt ctggtatttg attttgaatg ttttttaagt cagtggtgcc tttaggcaag
                                                                      932
                                                                      992
aactttcgaa attaatcatt ctttgtgttt tctgattttt caggtaacat gtacactatt
                                                                     1052
tagaaaccat catagtttat tcaccttaaa aaattgattg tattatttaa atatatcact
tagatgggca tttcctataa ttaggatatt ccaaatagtt gctgaaatca attgtgccat
                                                                     1112
                                                                     1161
tgaccaatgg atgcacttgg ttagccttaa ttttttyaaa aaaaaaaaa
<210> 332
<211> 363
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 57..311
<221> sig peptide
<222> 57..128
<223> Von Heijne matrix
      score 5.30000019073486
      seq LFHLLFLPHYIET/FK
<221> polyA signal
<222> 332..337
 <221> polyA site
<222> 351..363
 <400> 332
```

• •	
tgt tot cat goo too atg tot tit cac aca otg tio cat tig oto tio	107
Cys Ser His Ala Ser Met Ser Phe His Thr Leu Phe His Leu Leu Phe	
-20 -15 -10	255
ctc cca cat tac att gaa act ttc aag cct cag tcg aaa cat tgc ttc	155
Leu Pro His Tyr Ile Glu Thr Phe Lys Pro Gln Ser Lys His Cys Phe -5 1 5	
tto tgg ata gca gcc tto ttg aca tcc ctc ctc act ccc cag tcc cta	203
Phe Trp Ile Ala Ala Phe Leu Thr Ser Leu Leu Thr Pro Gln Ser Leu	
10 15 20 25	0.53
cag ggc ttc cat agc tct tta tgt gca ctt cga tcc cag cat ttt cca	251
Gln Gly Phe His Ser Ser Leu Cys Ala Leu Arg Ser Gln His Phe Pro 30 35 40	
tog act tgt aat tgt tto tgc tac ctg aca atc atc gcc ttg drd tac	299
Ser Thr Cys Asn Cys Phe Cys Tyr Leu Thr Ile Ile Ala Leu Xaa Tyr	
45 50 55	251
tgg gac aac ctt tgattactca ttatatcctc aataaatatt tgttgaacca	351
Trp Asp Asn Leu 60	
aaaaaaaaaa aa	. 363
0.00	
<210> 333 <211> 645	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 80232	
<221> sig_peptide	
<222> 80127	
<223> Von Heijne matrix	
score 3.7000004768372	
seq IALTLIPSMLSRA/AG	
<221> polyA_signal	
<222> 617622	•
<221> polyA_site	
<222> 634645	
<400> 333	
accttcttgt tatttatgct attctctttg tggctccatt cttcttcaa tcttctcagc	60
ttataaccgt ctttccctt atg cta agg ata gcc ctt aca ctc atc cca tct	112
Met Leu Arg Ile Ala Leu Thr Leu Ile Pro Ser	
-15 -10 atg ctg tca agg gct gct ggt tgg tgc tgg tac aag gag ccc act cag	160
Met Leu Ser Arg Ala Ala Gly Trp Cys Trp Tyr Lys Glu Pro Thr Gln	100
-5 1 5 10	
cag ttt tct tac ctt tgc ctg ccc tgc ctt tca tgg aat aar aaa ggc	208
Gln Phe Ser Tyr Leu Cys Leu Pro Cys Leu Ser Trp Asn Lys Lys Gly	
15 20 25	262
aac gtt ttg cag ctt cca aat ttc tgaaraaact aatctcarat tggcagttaa	262
Asn Val Leu Gln Leu Pro Asn Phe 30 35	
agtcaaaatg ttgccaaata tttattcctt ttgcctaakt ttggctaccc ggttcaattg	322
ctttttattt ttaatgtctt gactcttcar agttcgtacc tcaaaaraac aatgaraaca	382
tttgctttgc tttctgctga atccctaatc tcaacaatct atacctggac tgtccagttc	442
tectectgtg ctatettete ttetatecaa gtaraatgta ygeeaggare teetteete	502
tarcaattte tactaaaatg tccaagtara atgtttcctt ttacaatcaa attactgtat	562

622 ttattaattt qctaraatcc aktaaatcat tttggtagct ctggctgtgc tatcaataaa 645 aagatgaaag caaaaaaaaa aaa <210> 334 <211> 400 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 91..291 <221> sig\_peptide <222> 91..219 <223> Von Heijne matrix score 3.79999995231628 seq LISVLYLIPKTLT/TN <221> polyA\_signal <222> 367..372 <221> polyA site <222> 389..400 <400> 334 aacaaaagga gagttttata attcacttta aaaggagatt tgatggtaaa gtttaaagat ,60 taaaatattt tgttcttcaa ttacagagcg atg acc cca cag tat ctg cct cac 114 Met Thr Pro Gln Tyr Leu Pro His -40 162 ggt gga aaa tac caa gtt ctt gga gat tac tct ttg gca gtg gtc ttc Gly Gly Lys Tyr Gln Val Leu Gly Asp Tyr Ser Leu Ala Val Val Phe -35 -30 -25 ccc ctg cac ttt tct gat cta att tct gtt tta tac ctt ata ccc aaa 210 Pro Leu His Phe Ser Asp Leu Ile Ser Val Leu Tyr Leu Ile Pro Lys -15 -10 258 aca ctt act acc aac aca qct gtt aaa cat tct ata caa aaa aat tgt Thr Leu Thr Thr Asn Thr Ala Val Lys His Ser Ile Gln Lys Asn Cys atg mat ctg gta tta gga aaa tta ctt tca cag taaatatcaa agaaaaaaga 311 Met Xaa Leu Val Leu Gly Lys Leu Leu Ser Gln 20 371 ttaagggtct ctttgccatg cttttcatca tatgcaccaa atgtaaattt tgtacaataa 400 aattttattt cctaagyaaa aaaaaaaaa <210> 335 <211> 496 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 196..384 <221> sig\_peptide <222> 196..240

<223> Von Heijne matrix

score 6.69999980926514 sec ILSTVTALTFARA/LD

<221> polyA_signal	
<221> polyA_site <222> 485496	
<pre>&lt;400&gt; 335 aaaaaattgg teccagtttt caccetgeeg cagggetgge tggggaggge ageggtttag 6</pre>	C
attagccgtg gcctaggccg tttaacgggg tgacacgagc htgcagggcc gagtccaagg 12	
cccggagata ggaccaaccg tcaggaatgc gaggaatgtt tttcttcgga ctctatcgag 18	
gcacacagac agacc atg ggg att ctg tct aca gtg aca gcc tta aca ttt 23  Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe	
-15 -10 -5	
gcc aga gcc ctg gac ggc tgc aga aat ggc att gcc cac cct gca agt 27 Ala Arg Ala Leu Asp Gly Cys Arg Asn Gly Ile Ala His Pro Ala Ser 1 5 10	
gag aag cac aga ctc gag aaa tgt agg gaa ctc gag agc agc cac tcg 32	. 7
Glu Lys His Arg Leu Glu Lys Cys Arg Glu Leu Glu Ser Ser His Ser 15 20 25	
gcc cca gga tca'acc cag cac cga aga aaa aca acc aga aga	5
Ala Pro Gly Ser Thr Gln His Arg Arg Lys Thr Thr Arg Arg Asn Tyr 30 40 45	
30 35 40' 45 tet tea gee tgaaatgaak eegggateaa atggttgetg atearageee 42	: 4
Ser Ser Ala atattaaat tagaaaagtc aaattgasca ttattaaata aagcttgttt aatatgtctc 48	,
atatttaaat tggaaaagtc aaattgasca ttattaaata aagcttgttt aatatgtctc 48 aaacaaaaaa aa 49	
<210> 336	
<211> 968	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 54590	
<221> sig_peptide	
<222> 54227	
<pre>&lt;223&gt; Von Heijne matrix score 3.5</pre>	
seq GGILMGSFQGTIA/GQ	
<221> polyA site	
<222> 955965	
<400> 336	
atatttgccc cttactttat cttgtgcctt gagaaattgc tggggagaga ggt atg  Met	5 (
tcc act ggg cag ctg tac agg atg gag gat ata ggg cgt ttc cac tcc 10	٥,
Ser Thr Gly Gln Leu Tyr Arg Met Glu Asp Ile Gly Arg Phe His Ser	
cag cag cca ggt tcc ctc acc cca agc tca ccc act gtt ggg gag att	5:
Gln Gln Pro Gly Ser Leu Thr Pro Ser Ser Pro Thr Val Gly Glu Ile	
-40 -35 -30	
atc tac aat aac acc aga aac aca ttg ggg tgg att ggg ggt atc ctt 20	١
Ile Tyr Asn Asn Thr Arg Asn Thr Leu Gly Trp Ile Gly Gly Ile Leu	
-25 -20 -15 -10	
atg ggt tot tit dag gga acc att got gga daa ggo aca gga god acc	ż
Met Gly Ser Phe Gln Gly Thr Ile Ala Gly Gln Gly Thr Gly Ala Thr	

				-5					1				5				
														999		•	296
		10	•		_	-	15				+	20		Gly			
														atc			344
-	25					30					35			Ile			
														rgg			392
40		,	4 -		45					50				Xaa	55		
														tcc			440
Xaa	Gln	Gln	Pro	Asn 60	Gly	Ser	Leu	Ser	Leu 65	Asn	Ile	Ser	Ser	Ser 70	His		
														cct			488
			75			_		80					85	Pro			
														aaa			536
Arg	Xaa	Val 90	Cys	Ile	Asn	Pro	His 95	Pro	Pro	Pro	Pro	Ile 100	Leu	Lys	Xaa	•	
														999			584
Pro	Leu 105	Ser	Pro	Tyr	Pro	Lys 110	Pro	Gln	Leu	Gly	Thr 115	His	Ala	Gly	Gln		
gtc	aat	taad	caati	tta 1	tgcad	cagg	ta ct	tagti	tttai	t tgt	atta	accg	ttc	cagg	gta		640
Val 120	Asn																
															cctgta		700
															agacca		760
															tgtggt		820 880
															aaccca		940
			tttc	_	-			y Ly	CCaC	Lgeg	CLC	age	urg 9	ggcg	acagag	1	968
- ugg	Latt	·		aaaa	aa a		nem										300
<21	0> 3:	37															

<210> 337

<211> 901

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 133..846

<221> sig\_peptide

<222> 133..345

<223> Von Heijne matrix score 9.39999961853027 seq VVSFLLLLAGLIA/TY

<221> polyA\_site <222> 890..901

## <400> 337

		-40	,				-35	Ser				-30					
aag Lys	gaa Glu -25	tgg Trp	acc	tca Ser	aaa Lys	tta Leu -20	tgg Trp	cat His	cgt Arg	caa Gln	agc Ser -15	att Ile	gtg Val	gtg Val	tct Ser		315
ttt Phe -10	tta Leu	ctg Leu	ctg Leu	ctt Leu	gct Ala -5	ggg Gly	ctt Leu	ata Ile	gct Ala	acg Thr 1	tat Tyr	tat Tyr	gtt Val	gaa Glu 5	gga Gly		363
gtg Val	cat His	caa Gln	cag Gln 10	tat Tyr	gtg Val	caa Gln	cgt Arg	ata Ile 15	gag Glu	aaa Lys	cag Gln	ttt Phe	ctt Leu 20	ttg Leu	tat Tyr		411
gcc Ala	tac Tyr	tgg Trp 25	ata Ile	ggc	tta Leu	gga Gly	att Ile 30	ttg Leu	tct Ser	tct Ser	gtt Val	ggg Gly 35	ctt Leu	gga Gly	aca Thr	•	459
ggg Gly	ctg Leu 40	cac His	acc Thr	ttt Phe	ctg Leu	ctt Leu 45	tat Tyr	ctg Leu	ggt Gly	cca Pro	cat His 50	ata Ile	gcc Ala	tca Ser	gtt Val	•	507
aca Thr 55	tta Leu	gct Ala	gct Ala	tat Tyr	gaa Glu 60	tgc Cys	aat Asn	tca Ser	gtt Val	aat Asn 65	ttt Phe	ccc Pro	gaa Glu	cca Pro	ccc Pro 70		555
								gat Asp					Glu				603
att Ile	tct Ser	ttg Leu	tgg Trp 90	agt Ser	atc Ile	atc Ile	tca Ser	aaa Lys 95	gtt Val	agg Arg	att Ile	gaa Glu	gcc Ala 100	tgc Cys	atg Met		651
tgg Trp	ggt Gly	atc Ile 105	ggt Gly	aca Thr	gca Ala	atc Ile	gga Gly 110	gag Glu	ctg Leu	cct Pro	cca Pro	tat Tyr 115	ttc Phe	atg Met	gcc Ala		699
aga Arg	gca Ala 120	gct Ala	cgc Arg	ctc Leu	tca Ser	ggt Gly 125	gct Ala	gaa Glu	cca Pro	gat Asp	gat Asp 130	gaa Glu	gag Glu	tat Tyr	cag Gln		747
Glu 135	Phe	Glu	Glu	Met	Leu 140	Glu	His	Ala	Glu	Ser 145	Ala	Gln	Val	Arg	aca Thr 150		795
gtg Val	ggg ggg	ata Ile	gaa Glu	aat Asn 155	aga Arg	aca Thr	ctt Leu	tac Tyr	ttc Phe 160	Phe	cta Leu	aag Lys	agg Arg	cta Leu 165	tta Leu		843
agg Arg	taa	aatt	gtt	agta	gtta	ct c	tgaa	gaag	a aa	actg	ctaa	agt	aaaa	aaa	aaaaa		901

```
<210> 338
```

<213> Homo sapiens

<220>

<221> CDS

<222> 138..671

<221> sig\_peptide

<222> 138..248

<223> Von Heijne matrix score 3.5

seq LVFNFLLILTILT/IW

<221> polyA\_signal

<222> 1319..1324

<221> polyA\_site

<sup>&</sup>lt;211> 1347

<sup>&</sup>lt;212> DNA

## <222> 1338..1347

<400	)> 33	8 8								•					•	
aaga	atgo	tt q	gtgaa	agtag	gc aa	actaa	agto	g gca	agtgi	tttc	ttc	tgaa	att	ctca	ggcagt	60
															aggaat	120
CCC	agaa	aga d	ctggg	gga a	atg g	gag a	iga d	cag t	tca a	agg g	gtt a	atg	tca	gaa a	aag	170
				1	1et C	Blu <i>P</i>	arg (	3ln S	Ser A	Arg V	Val I	Met	Ser	Glu 1	Lys	
							∙35					-30				
gat	gag	tat	cag	ttt	caa	cat	cag	gga	gcg.	gtg	gag	ctg	ctt	gtc	ttc	218
Asp	Glu	Tyr	Gln	Phe	Gln	His	Gln	Gly.	Ala	Val	Glu	Leu	Leu	Val	Phe	
_	-25	_		٠,		-20					-15	•				
aat	ttt	ttg	ctc	atc	ctt	acc	att	ttg	aca	atc	tgg	tta	ttt	aaa	aat	266
Asn	Phe	Leu	Leu	Ile	Leu	Thr	Ile	Leu	Thr	Ile	Trp	Leu	Phe	Lys	Asn	•
-10					-5					1				5		
cat	cga	ttc	cgc	ttc	ttg	cat	gaa	act	gga	gga	gca	atg	gtg	tat	ggc	314
His	Arg	Phe	Arg	Phe	Leu	His	Glu	Thr	Gly	Gly	Ala	Met	Vál	Tyr	Gly	
	_		10					15					20			
ctt	aya	atg	gga	cta	att	tta	csa	tat	gct	aca	gca	cca	act	gat	att	362
														Asp		
		25					30	7		•		35		_		
gaa	agt	aar	rct	atc	tat	gac	tat	qta	aaa	cta	act	ttc	agt	cca	tca	410
														Pro		
	40	1			- ] -	45	-7-		-2-		50			•		•
act		cta	att	aat	atc		gac	caa	att	tat		tat	aaa	tac	aar	458
														Tyr		
55			•	11011	60			<b></b>		65		-,-	-7-	-2-	70	
	maa.	ata	agt	cad		amc	atc	aat	cct		cam	gga	aat	gct	ata	506
														Ala		
T.A	GIU	116	261	75	1113	Naa	110	Poli	80	1113	Auu	Ory	,70	85		
c++	<b>~</b> 22	224	ata	75	+++	cat	cca	ros		ttc	ttc	aat	att	tta	cta	554
														Leu		
Dea	GIU	шys	90	1111	FIIC		FIO	95	110	FIIC	FIIC	Abii	100		200	
	~~~	2++		+++	a > t	ac.	~~~		agt	cta	220	220		cac	+++	602
														His		002
PIU	PIO		TTE	PHE	пть	Ala	110	ıyı	261	Deu	шуъ	115	Ar 9	1115	1110	
		105				-++			+-+	~~~	++-		~~~	act	acc	650
														act		050
Pne		ASN	ьeu	GIÀ	Ser		ьeu	Thi	ıyı	Ala		neu	GIY	Thr	MIG	
	120			_4_		125					130				_	701
		_					taa	gtga	cat	cegg.	aget	ca a	gttg	cagg	L	701
	ser	Cys	Ile	vai		GIA										
135					140											761
ggc	rgrg	999	rcyg	tgat	ct g	tgtg	aggg	a tc	taac	actt	cca	ggat	tct	tget	ggckgg	761
															ttccac	821
															tttctc	881
															tgaagc	941
															tttgtc	1001
															caagag	1061
															atatca	1121
															actctt	1181
															actctg	1241
													aat	ccag	cctctg	1301
ata	atcc	cgt	ccaa	taca	tt a	aagc	tcca	c tg	cagg	aaaa	aaa	aaa				1347

<sup>&</sup>lt;210> 339

<sup>&</sup>lt;211> 987

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;220>

<sup>&</sup>lt;221> CDS

<222> 124..411 <221> sig\_peptide <222> 124..186 <223> Von Heijne matrix score 6.30000019073486 seq MVALCCCLWKISG/CE <221> polyA signal <222> 948..953 <221> polyA\_site <222> 971..983 .<400> 339 60 aagacgctgc ctttagggag agataaaaag cataatgaca ttagctagga aagttaattt 120 tcagttctta ctgaagtgct gtatgaaact gaaatttcca aggaactgaa ttttgtgagc 168 caa atg agc atg caa ttc ttg ttt aag atg gtg gcc tta tgc tgt tgt Met Ser Met Gln Phe Leu Phe Lys Met Val Ala Leu Cys Cys -15 -10 216 ctc tgg aag atc tcc ggc tgt gag gaa gtc cct cta act tac aac ctg Leu Trp Lys Ile Ser Gly Cys Glu Glu Val Pro Leu Thr Tyr Asn Leu -5 264 ctc aag tgc ctc cta gat aaa gcg cac tgt gta ctc ctg aca cct tgt Leu Lys Cys Leu Leu Asp Lys Ala His Cys Val Leu Leu Thr Pro Cys 20 312 ggt tac atc ttt tcc ttg atc agt cca gaa att ctc aaa ctc act tta Gly Tyr Ile Phe Ser Leu Ile Ser Pro Glu Ile Leu Lys Leu Thr Leu 30 360 atc act ttg cav atc ctc tta ata ctc aaa aat cta cac tta ctg tgg Ile Thr Leu Xaa Ile Leu Leu Ile Leu Lys Asn Leu His Leu Leu Trp 45 50 408 ctg aca gtt tca agc awa tgt gtt cat cgc agt agt gca aga aaa gaa Leu Thr Val Ser Ser Xaa Cys Val His Arg Ser Ser Ala Arg Lys Glu 65 70 aag tagaagaacc ctgcagagat ttgatggaac ccagcttcta ttcattaaaa 461 Lys 75 521 ccaatggcaa aatataaagc aaataggagg tgacgaaggt tacaaaaata cgtattgttt 581 atgttttccc tggggtgtgc tgattgtcag gcatcagttc cctgtgccat tcattcccca acacagcatg catcagaaat tttatcaata aatgctttct ctctcaatgt tcaacctatg 641 ctgatagacc attaaataca gtttttgggt tcacagcttg tcatcatcat ttgtctatac 701 761 ctgtggcaaa gaatatctaa taagatactc tcagcatttt gcacacttaa actaagatgc 821 tgaatgctgt attttacgga ataatcagcc acattaaatt tggagactca acaagcatgc tgtgaacatt caacattagg tttaaatttt atttttaaaa gttaataata aaaggatata 881 941 tgttaagtat tatgaaaccc tgcatatact gtaataaaat ggtggatgtg aatggacaat 987 atatgcaata aaatttataa tttgattcya aaaaaaaaa aamccv

```
<210> 340

<211> 748

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 372..494

<221> sig peptide
```

<223> Von Heijne matrix

<222> 372..443

score 5.30000019073486 seq RILLLHFYCLLRS/SE

<221> polyA\_signal <222> 708..713 <221> polyA site <222> 732..745 <400> 340 '; acatgaaatg tgcttggtct gtgatctctt ggtcagatat ctgccttcca ggcgatcctt 60 120 tgaggttgtg taattcagct ggccctggct cctggtccct gttactgagc tgggcagtcg aaccgaaggc agatgagctc aagatcatgc cttgggaagc atggtgctct aggggtgcct 180 240 ttttattcct ttcattgtat tatagactgt ttccaagttt atggttagaa atggtaaagt gggtctggtg ttttgaggta gaacccagcc tagggcaaga tatgaactgt tcttgaggta 300 gaaatgtcta cagtcagttg tttcatctag cttgcatctt aaaacacaaa cccttcagtt 360 gettteactt a atg cae aca ttt gee aat gae aga ggg tta tae agg ate 410 Met His Thr Phe Ala Asn Asp Arg Gly Leu Tyr Arg Ile -20 458 ctt ctt tta cat ttc tat tgt ctg cta cgc tca tca gag tat att ttg Leu Leu His Phe Tyr Cys Leu Leu Arg Ser Ser Glu Tyr Ile Leu -10 -5 ggg tac aag gtt ttg ggg gtt ttt tty ccc att ttg taactgcctt 504 Gly Tyr Lys Val Leu Gly Val Phe Phe Pro Ile Leu attgaaaadt aaktgeeett eeatteeagg eeteeteata ttgtaettgt tteetgeeaa atctggggga tcatttgtat tttaactttg taatctatgg ctctgtactg ttgaaagstc 624 tcaattctgt ggggtctcct tagtatgtat gtgacttttc atgttgcaat atcacacgat 684 744 gggatggccc gacttttgct cttaataaat aatctgaatg agtaagaraa aaaaaaaaaa 748 accc

<210> 341

<211> 1106

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 112..450

<221> sig peptide

<222> 112..192

<223> Von Heijne matrix
 score 7.19999980926514
 seq SLLFFLLLEGGXT/EQ

<221> polyA signal

<222> 1053..1058

<221> polyA\_site

<222> 1095..1106

<400> 341

aagacctcgg aacgagagcg ccccggggag ctcggagcgc gtgcacgcgt ggcavacgga 60 gaaggcvakk rcnnnnrctt gaaggttctg tcaccttttg cagtggtcca a atg aga 117

Met Arg

raa aag tgg aaa atg gga ggc atg aaa tac atc ttt tcg ttg ttc 165

Xaa Lys Trp Lys Met Gly Gly Met Lys Tyr Ile Phe Ser Leu Leu Phe

-25 -20 -15 -10

ttt ctt ttg cta gaa gga ggc kaa aca gag caa gtr amn cat tca gag 213

														_	<b>61</b>	
Phe	Leu	Leu	Leju	Glu -5	Gly	Gly	Xaa	Thr	Glu 1	Gln	Val	Xaa	His 5	Ser	Glu	
aca	tat	tac	atq	ttt	caa	gac	aag	aag	tac	aga	gtg	ggt	gag	aga	tgg	261
Thr	Tyr	Cys	Met	Phe	Gln	Asp	Lys	Lys	Tyr	Arg	Val	GTA	Glu	Arg	Trp	
		10					15					20		+	ato	309
cat	cct	tac	ctg	gaa	cct	tat	999	ttg	gtt	tac	tgc	gtg	aac	tgc	TIO	305
His	Pro 25	Tyr	Leu	Glu	Pro	Tyr 30	Gly	Leu	Val	Tyr	Cys 35	Val	ASN	Cys	116	
- ~ ~	# C D	asa	aat	aaa	aat	ata	ctt	tac	agc	cqa	qtc	aga	tgt	cca	aat	357
Cyc	Car	Glu	Δen	GJA	Asn	Val	Leu	Cvs	Ser	Arg	Val	Arg	Cys	Pro	Asn	
40	JCI	Gru	V Dir	017	45			٠.		50		_			55	
~++	cat	tac	ctt	tct	cct	ata	cat	att	cct	cat	ctg	tgc	tgc	cct	cgc	405
Val	His	Cvs	Leu	Ser	Pro	Val	His	Ile	Pro	His	Leu	Cys	Cys	Pro	Arg	
Val		O, D		60					65					70		
tac	cca	gaa	gac	tcc	tta	ccc	cca	gtg	aac	aat	rwg	gtg	acc	agc		450
Cvs	Pro	Glu	Asp	Ser	Leu	Pro	Pro	Val	Asn	Asn	Xaa	Val	Thr	Ser		•
_			<b>\75</b>					80					85			
tag	tett	ack	agta	caat	aa a	acaa	ctta	с са	acat	ggas	agc	tgtt	cgt	agct	grrggg	510
ctc	tttc	aga	atica	acaa	cc c	matc	aatq	c ac	ccag	tgca	gct	gttc	gga	rgga	aackty	570
tat	tata	atc	tcaa	gact	ta c	ccca	aatt	a ac	ctgt	gcct	tcc	cagt	CTC	tgtt	CCarac	630
tcc	tact	acc	aaat.	wtac	acia	rgag	atgg	a ca	actg	tcat	999	aacm	ttc	tgat	ggrgar	690
atc	ttcc	aac	aacc	tacc	aa c	agag	aagc	a ag	acat	tctt	acc	accg	CCC	CCac	Laigai	750
cct	ccac	caa	acca	acad	ac t	qqaq	qtct	g to	ccgc	tttc	ctg	gggc	cag	aagt	caccyy,	810
gga	actic	tta	tigga	ttcc	ca q	caaq	catc	a gg	aacc	attg	tgc	aaat	tgt	catc	aataac	870
222	caca	agc	ataa	acaa	at a	tqtq	tttc	c aa	.tgga	aaga	CCT	atto	tca	tggc	gagicc	930
taa	cacc	caa	acct	ccaa	ac a	tttc	gcat	t gt	ggag	itgtg	tgc	tatg	tac	ttgt	aatgtt	990
acc	aago	aad	agto	taaq	aa a	atco	actg	C CC	caat	cgat	acc	cctg	caa	gtat	CCLCaa	1050
aaa	ataq	acq	gaaa	atgo	tg c	aagg	ıtgtg	t co	aggt	aaaa	aag	caaa	aaa	aaaa	aa	1106
	_	_		, ,	_							•				
				•												

```
<210> 342
<211> 1191
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 117..866
<221> sig_peptide
<222> 117..170
<223> Von Heijne matrix
      score 10.6999998092651
      seq LILLALATGLVGG/ET
<221> polyA_signal
<222> 1159..1164
<221> polyA_site
<222> 1178..1190
<400> 342
```

														999 Gly 30		263
				ccc					aca					ctc Leu		311
														gag Glu		359
														ccc Pro		407
			_					_		_		_		atg Met	_	455
														ccc Pro 110		503
				_	_	_		_			_	_		att Ile		551
														acc Thr		. 599
_	_	_								_	_	_		aac Asn	_	647
						_		-		_	_			cag Gln		695
														gtc Val 190		743
														tgt Cys		791
		_	_			-				_				gtg Val		839
			gag Glu		_	_			tag	actg	gac (	ccac	ccac	ca		886
cag	ccca	tca	ccct	ccat	tt c	cact	tggt	g tt	tggti	tcct	gtt	cact	ctg	ttaai	taagaa	946
															atgctg	1006
															gccttg	1066
															agcccc	1126
															aaaaa	1186
aaa							_				•					1191

<210> 343

<211> 1070

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 13..465

<221> sig\_peptide <222> 13..75

<223> Von Heijne matrix
score 3.90000009536743
seq PVAVTAAVAPVLS/IN

<221> polyA\_signal <222> 1035..1040

<221> polyA\_site <222> 1060..1070

<400> 343

agagtcggga aa atg gct gcg agt acc tcc atg gtc ccg gtg gct gtg acg Met Ala Ala Ser Thr Ser Met Val Pro Val Ala Val Thr -15 -20 gcg gca gtg gcg cct gtc ctg tcc ata aac agc gat ttc tca gat ttg 99 Ala Ala Val Ala Pro Val Leu Ser Ile Asn Ser Asp Phe Ser Asp Leu **\-**5 cgg gaa att aaa aag caa ctg ctg ctt att gcg ggc ctt acc cgg gag 147 Arg Glu Ile Lys Lys Gln Leu Leu Leu Ile Ala Gly Leu Thr Arg Glu 15 cgg ggc cta cta cac agt agc aaa tgg tcg gcg gag ttg gct ttc tct 195 Arg Gly Leu Leu His Ser Ser Lys Trp Ser Ala Glu Leu Ala Phe Ser 35 25 ctc cct gca ttg cct ctg gcc gag ctg caa ccg cct ccg cct att aca 243 Leu Pro Ala Leu Pro Leu Ala Glu Leu Gln Pro Pro Pro Pro Ile Thr 50 gag gaa gat gcc cag gat atg gat gcc tat acc ctg gcc aag gcc tac 291 Glu Glu Asp Ala Gln Asp Met Asp Ala Tyr Thr Leu Ala Lys Ala Tyr 60 65 339 ttt gac gtt aaa gag tat gat cgg gca gca cat ttc ctg cat ggc tgc Phe Asp Val Lys Glu Tyr Asp Arg Ala Ala His Phe Leu His Gly Cys 80 387 aat gca aga aaa gcc tat ttt ctg tat atg tat tcc aga tat ctg gtg Asn Ala Arg Lys Ala Tyr Phe Leu Tyr Met Tyr Ser Arg Tyr Leu Val 100 95 435 agg gcc att tta aaa tgt cat tct gcc ttt agt gaa aca tcc ata ttt Arg Ala Ile Leu Lys Cys His Ser Ala Phe Ser Glu Thr Ser Ile Phe 115 110 aga acc aat gga aaa gtt aaa tct ttt aaa tagcttagca gtgggccact 485 Arg Thr Asn Gly Lys Val Lys Ser Phe Lys 125 545 gaatgaatgt actttataca tagcaataat aaaaaaaaga tatcataaat aaagttaaaa aggatggtaa aaaaaaaat attcttagga atgactaaca ggataagtaa caacctgatt atttatttac tttaggttat ataaggttct tcatgcctgt gaattaatat tattgtgtaa 665 gaattaagtt aaaaagcctg ggctgacttt taaatttata aattcattta tcatgtttat 725 agtatattta ttgtttttct ttcatggcta ttaaaaagta tgactgtaaa ggacaatgca 785 agtaaaccaa cttaatactg tattgaataa taagtacaat ttattatttt actttgaaac 845 attatgaatt tactttccta ctttttctta gttgttatct atataaattg attaaaaaaa 905

cattttatgt acttctcatt tcctagtaca ggttgagtat cccttatttg aagtgcttgg

gaccaaaagt gtttcagatt tcagattttt ttcagatttt ggtatatttg cattatactt

actggttgaa ataaaaaatg ctgcagtgag tgtcaaaaaa aaaaa

965 1025

1070

<210> 344

<211> 1213

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 2..718

WO 99/31236 -260- PCT/IB98/02122

<221> sig peptide <222> 2..76 <223> Von Heijne matrix score 3.90000009536743 seg RVGLLLGGGGVYG/SR <221> polyA signal <222> 1170..1175 <221> polyA\_site. <222> 1203..1213 <400> 344 a atg ccc cgg aag cgg aag tgc gat ctt cgg gct gtc aga gtt ggt ctg 49 Met Pro Arg Lys Arg Lys Cys Asp Leu Arg Ala Val Arg Val Gly Leu -15 -20 97 tta ctc ggt ggc gga gtc tac gga agc cgt ttt cgc ttc act ttt Leu Leu Gly Gly Gly Val Tyr Gly Ser Arg Phe Arg Phe Thr Phe 1 .<del>-</del> 5 cct ggc tgt aga gcg ctt tcc ccc tgg cgg gtg aga vtg cag aga cga 145 Pro Gly Cys Arg Ala Leu Ser Pro Trp Arg Val Arg Xaa Gln Arg Arg 15 agg tgc gag atg agc act atg ttc gcg gac act ctc ctc atc gtt ttt . 193 Arg Cys Glu Met Ser Thr Met Phe Ala Asp Thr Leu Leu Ile Val Phe 30 ate tet gtg tge acg get etg ete gea gag gge ata ace tgg gte etg 241 Ile Ser Val Cys Thr Ala Leu Leu Ala Glu Gly Ile Thr Trp Val Leu 45 50 289 gtt tac agg aca gac aag tac aag aga ctg aag gca gaa gtg gaa aaa Val Tyr Arg Thr Asp Lys Tyr Lys Arg Leu Lys Ala Glu Val Glu Lys 65 cag agt aaa aaa ttq gaa aag aag gaa aca ata aca gag tca gct 337 Gln Ser Lys Lys Leu Glu Lys Lys Glu Thr Ile Thr Glu Ser Ala 75 . 80 385 ggt cga caa cag aaa aar aaa ata gag aga cdd kaa kas amc ctg arg Gly Arg Gln Gln Lys Lys Ile Glu Arg Xaa Xaa Xaa Xaa beu Xaa aat aac aac aga gat cta tca atg gtt cga atg aaa tcc atg ttt gct 433 Asn Asn Asn Arg Asp Leu Ser Met Val Arg Met Lys Ser Met Phe Ala 110 115 att ggc ttt tgt ttt act gcc cta atg gga atg ttc aat tcc ata ttt 481 Ile Gly Phe Cys Phe Thr Ala Leu Met Gly Met Phe Asn Ser Ile Phe 125 130 529 gat ggt aga gtg gtg gca aag ctt cct ttt acc cct ctt tct tas rtc Asp Gly Arg Val Val Ala Lys Leu Pro Phe Thr Pro Leu Ser Xaa Xaa 140 145 sra gga ctg tct cat cga aat ctg ctg gga gat gac acc aca gac tgt 577 Xaa Gly Leu Ser His Arg Asn Leu Leu Gly Asp Asp Thr Thr Asp Cys 155 160 625 tcc ttc att ttc ctg taw att ctc tgt act atg tcg att cga cag aac Ser Phe Ile Phe Leu Xaa Ile Leu Cys Thr Met Ser Ile Arg Gln Asn 175 att cag aag att ete gge ett gee eet tea ega gee gee ace aag eag 673 Ile Gln Lys Ile Leu Gly Leu Ala Pro Ser Arg Ala Ala Thr Lys Gln 185 190 195 718 gca ggt gga ttt ctt ggc cca cct cct tct ggg aag ttc tct Ala Gly Gly Phe Leu Gly Pro Pro Pro Pro Ser Gly Lys Phe Ser 205 210 tgaactcaag aactctttat tttctakcat tctttctaga cacacaca tcagactggc 778 aactgttttg tascaagagc cataggtagc cttackactt gggcctcttt ctagttttga 838 898 attatttcta agccttttgg gtatkattag agtgaaaatg gcagccagca aacttgatag

• •	
tgcttttggt cctagatgat ttttatcaaa taagtggatt gattagttaa gttcaggtaa tgtttatgta atgaaaaaca aatagcatcc ttcttgttc atttacataa gtattttctg tgggaccgac tctcaaggca ctgtgtatgc cctgcaagtt ggctgtctat gagcatttag agatttagaa gaaaaattta gtttgtttaa cccttgtaac tgtttgttt gttgtttttttttt	958 1018 1078 1138 1198 1213
<210> 345 <211> 978 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 86709	
<221> sig_peptide <222> 86361 <223> Von Heijne matrix score 6.30000019073486 seq LLMSILALIFIMG/NS	
<221> polyA_signal <222> 943948	
<221> polyA_site <222> 963973	
<400> 345	
aaagcateet teeetaggae tgetgtaage tttgageete tageaggaga catgeetegg ggaegaaaga gteggegeeg eegta atg ega gag eeg eag aag aga aee gea Met Arg Glu Pro Gln Lys Arg Thr Ala	60 112
aca atc gca aaa tyc rrg gcs tva gag ggc ctc cga gac ccc tat ggc Thr Ile Ala Lys Xaa Xaa Ala Xaa Glu Gly Leu Arg Asp Pro Tyr Gly -80 -75 -70	160
cgc ctc tgt ggt agc gag cac ccc cga aga cca cct gag cgg ccc gag Arg Leu Cys Gly Ser Glu His Pro Arg Arg Pro Pro Glu Arg Pro Glu	208
gaa gac ccg agc act cca gag gag gcc tct acc acc cct gaa gaa gcc Glu Asp Pro Ser Thr Pro Glu Glu Ala Ser Thr Thr Pro Glu Glu Ala	256
-50 -45 -40  tcg agc act gcc caa gca caa aag cct tca gtg ccc cgg agc aat ttt  Ser Ser Thr Ala Gln Ala Gln Lys Pro Ser Val Pro Arg Ser Asn Phe  -35 -20 -25	304
cag ggc acc aag aaa agt ctc ctg atg tct ata tta gcg ctc atc ttc Gln Gly Thr Lys Lys Ser Leu Leu Met Ser Ile Leu Ala Leu Ile Phe -15 -10 -5	352
atc atg ggc aac agc gcc aag gaa gct ctg gtc tgg aaa gtg ctg ggg Ile Met Gly Asn Ser Ala Lys Glu Ala Leu Val Trp Lys Val Leu Gly 1 5 10	400
aag tta gga atg cag cct gga cgt cas cac agc atc ttt gga gat ccg Lys Leu Gly Met Gln Pro Gly Arg Xaa His Ser Ile Phe Gly Asp Pro 15 20 25	448
aag aar atc gtc aca gaa ran ttt gtg cgc aga ggg tac ctg att tat Lys Lys Ile Val Thr Glu Xaa Phe Val Arg Arg Gly Tyr Leu Ile Tyr 30 35 40 45	496
ara ccg gtg ccc cgt abc agt ccg gtg gag tat gas ttc ttc tgg ggg Xaa Pro Val Pro Arg Xaa Ser Pro Val Glu Tyr Xaa Phe Phe Trp Gly 50 55 60	544

WO 99/31236 -262- PCT/IB98/02122 -

CCC cga gca cac gtg gaa tcg agc ara ctg aaa stc wtg cat ttt gtg Pro Arg Ala His Val Glu Ser Ser Xaa Leu Lys Xaa Xaa His Phe Val 65 70 75	592
gca agg gtt cgt aac cga tgc tct aaa gac tgg cct tgt aat tat gac Ala Arg Val Arg Asn Arg Cys Ser Lys Asp Trp Pro Cys Asn Tyr Asp 80 85 90	640
tgg gat tcg gac gat gat gca gag gtt gag gct atc ctc aat tca ggt Trp Asp Ser Asp Asp Asp Ala Glu Val Glu Ala Ile Leu Asn Ser Gly	688
gct arg ggt tat tcc gcc cct taagtaratc tgaggcagac ccttgggggt Ala Xaa Gly Tyr Ser Ala Pro	739
gtaaaagaga gtcacaggta ccccaaggag tagatgccag ggtcctaagt tgaaaatgmt gtcgattggg ggcgggggac actgtatttg atatttgtga tcagtgatca ttgttcaact	799 859
gcgaaataga gtgtttgctt ttgataatgg aaaattgtat tcgttttaaa attccgtttg ttgagaataa caatatgttt aaaaatataa ttgaacaaat tttaaaaaaa aaaamcccy	919 978
<210> 346	
<211> 810	
<212> DNA <213> Homo sapiens	
<220> <221> CDS	
<222> 63320	
<221> sig_peptide <222> 63179	•
<223> Von Heijne matrix	
score 3.9000009536743 seq VLAIGLLHIVLLS/IP	
<221> polyA_signal	
<221> polyA_site <222> 799810	•
<400> 346	60
agggaaccga tcccgggccg ttgatcttcg gccccacacg aacagcagag aggggcatca gg atg aat gtk ggc aca gcg cac ags dag gtg aac ccc aac acg cgg Met Asn Val Gly Thr Ala His Xaa Xaa Val Asn Pro Asn Thr Arg	60 107
-35 -30 -25 gtk atg aac agc cgt ggc atc tgg ctc tcc tac gtg ctg gcc atc ggt	155
Val Met Asn Ser Arg Gly Ile Trp Leu Ser Tyr Val Leu Ala Ile Gly -20 -15 -10	
ctc ctc cac atc gtg ctg ctg agc atc ccg ttt gtk agt gtc cct gtc Leu Leu His Ile Val Leu Leu Ser Ile Pro Phe Val Ser Val Pro Val	203
gtc tgg acc ctc acc aac ctc att cac aac atg ggc atg tat atc ttc Val Trp Thr Leu Thr Asn Leu Ile His Asn Met Gly Met Tyr Ile Phe 10 15 20	251
ctg cac acg gtg aag ggg aca ccc ttt gag acc ccg gac cag ggc aag Leu His Thr Val Lys Gly Thr Pro Phe Glu Thr Pro Asp Gln Gly Lys	299
30 35 40  gcg agg ctg cta acc cac tgg tgagcagatg gattatgggg tccagttcac  Ala Arg Leu Leu Thr His Trp	350
45	4
ggcctctcgg aakttcttga ccatcacacc catcgtgctg tacttcctca ccagcttcta cactaaktac raccaaatcc attttgtgct caacaccgtg tccctgatra gcgtgcttat	410 470

ccccaagctg ccccagctcc acggaktccg gat cascccettc ccctgcccag ggtggcaggg gag chctgaaaac araaaraara rscctctgga caccctaatttcc cccctcgctt cccccagtag cca ggtaggcccc ctgggctctg accttttctg aat aatararact ccatggagtt ggtcatggaa aaa	tgggtagg gtaaaaggca tktgctgcaa 330 tgccara ratgggggtt gagcctctgg 650 acttgga gtagcttgta ytggggttgg 710 tttttga tcttttcctt ttgctttttg 770
<210> 347	
<211> 771	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 299418	
<221> sig_peptide	
<222> 299379 <223> Von Heijne matrix	•
score 3.59999990463257	
seq LTLLLITPSPSPL/LF	
-	
<221> polyA_signal	
<222> 739744	•
<221> polyA_site	
<222> 762771 · ·	•
<400> 347	respective toggetting tatagatogs 60
accttgggct ccaaattcta gctcataaag at	caageke egeaaceeee easuals
taagaaaaga gcaagctgtc cagagagtga gaaaatgatgtc catttgagcc ccaccacgga gg	igitigaa aagagagges easaasas
aaatgatgtc catttgagcc ccattatgga gg	racticin cattgatten cittacacaa 240
ctggcattta gtctgcatta cacaaataga ca	ctaattta tttggaacaa gcagcaaa 298
ard aga act tha tht ggt gca gtc agg	get eea tit agt tee ete act 340
Met Arg Thr Leu Phe Gly Ala Val Arg	Ala Pro Phe Ser Ser Leu Thr
-25 -20	-15
ctg ctt cta atc acc cct tct ccc agc	cct ctt cta ttt gat aga ggt 394
Leu Leu Leu Ile Thr Pro Ser Pro Ser	
-10 -5 ctg tcc ctc aga tca gca atg tct tag	<b>-</b>
Leu Ser Leu Arg Ser Ala Met Ser	
10	
offggractc atticticta actititaata aa	catttagg tataatacat tacagtaagt 50
gctatttaga tacaaactta aaacatacta ta	tattttaa ggatctaaga atcctttara 56
rrrggcacat gactgaagta cctcagctgc gc	agcotgta accagttott toaatgladd 62
agtagraato ccaoccttaa cctabccctg ca	rataaaag ctaactttta ttaataccag 68
ccctgaataa tggcactaat ccacactctt cc	ttaragtg atgctggaaa aataaaatca 74
ggggcttcag attaaaaaaa aaa	• •

<210> 348 <211> 409 <212> DNA <213> Homo sapiens <220> <221> CDS

<222> 186..380

<222> 186233	
<223> Von Heijne matrix	
score 4	
seg FFLFLSFVLMYDG/LR	
•	
<221> polyA signal	
<222> 383388	
<pre>&lt;221&gt; polyA_site</pre>	
<222> 396409	
•	
<400> 348	
ataaaagaag cagcaaatag aatttcccac aaagtaagtt gactctaaat cttaagtatt	60
acctagtttt ttaaaggttt gaatataata atgcagtatt tgcagtataa aaaggaagga	120
attigtagag aatcatitig gigcicaagi cicitagcag igccitatig ccicatagca	180
agaag atg ctg ggg ttt ttt ttg ttt ttg tcc ttt gta tta atg tat gat	230
Met Leu Gly Phe Phe Leu Phe Leu Ser Phe Val Leu Met Tyr Asp	
-15 -10 -5	
ggt ttg cgc ctt ttt ggc att ctt tca aca tgt cgt gta cat cac acc	278
The law has too the give all the car and the give year the the alle	. 2/0
Gly Leu Arg Leu Phe Gly Ile Leu Ser Thr Cys Arg Val His His Thr	
1 5 10 15	
atg aat cag tic cta att gat ata tot ago tit acc too oga git aaa.	326
Met Asn Gln Phe Leu Ile Asp Ile Ser Ser Phe Thr Ser Arg Val Lys	
20 25 30	
aaa aaa atc ttt tta ttt tat gcc ttc awa ggt tgc ycg ttt car agt	274
	374
Lys Lys Ile Phe Leu Phe Tyr Ala Phe Xaa Gly Cys Xaa Phe Gln Ser	
35 40 45	
gcc aca taaataaaat gtttaacaaa aaaaaaaaa	409
Ala Thr	
·	
<210> 349	
<210> 349 <211> 613	
•	
<211> 613 <212> DNA	
<211> 613	
<211> 613 <212> DNA <213> Homo sapiens	
<211> 613 <212> DNA <213> Homo sapiens <220>	
<211> 613 <212> DNA <213> Homo sapiens <220> <221> CDS	
<211> 613 <212> DNA <213> Homo sapiens <220>	
<211> 613 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69458	
<211> 613 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 69458	
<pre>&lt;211&gt; 613 &lt;212&gt; DNA &lt;213&gt; Homo sapiens &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458 &lt;221&gt; sig_peptide</pre>	
<pre>&lt;211&gt; 613 &lt;212&gt; DNA &lt;213&gt; Homo sapiens &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458 &lt;221&gt; sig_peptide &lt;222&gt; 69233</pre>	
<pre> &lt;211&gt; 613 &lt;212&gt; DNA &lt;213&gt; Homo sapiens &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458 &lt;222&gt; 69233 &lt;223&gt; Von Heijne matrix</pre>	
<pre> &lt;211&gt; 613 &lt;212&gt; DNA &lt;213&gt; Homo sapiens &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458 &lt;222&gt; 69233 &lt;223&gt; Von Heijne matrix</pre>	
<pre> &lt;211&gt; 613 &lt;212&gt; DNA &lt;213&gt; Homo sapiens &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458 &lt;222&gt; 69233 &lt;223&gt; Von Heijne matrix</pre>	
<pre> &lt;211&gt; 613 &lt;212&gt; DNA &lt;213&gt; Homo sapiens &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458 &lt;222&gt; 69233 &lt;223&gt; Von Heijne matrix</pre>	
<pre> &lt;211&gt; 613 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458 </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 69233 </pre> <pre> &lt;223&gt; Von Heijne matrix</pre>	
<pre> &lt;211&gt; 613 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458 </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 69233 </pre> <pre> &lt;223&gt; Von Heijne matrix</pre>	
<pre> &lt;211&gt; 613 &lt;212&gt; DNA &lt;213&gt; Homo sapiens </pre> <pre> &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458 </pre> <pre> &lt;221&gt; sig_peptide &lt;222&gt; 69233 </pre> <pre> &lt;223&gt; Von Heijne matrix</pre>	
<pre> 221&gt; 613</pre>	
<pre> &lt;211&gt; 613 &lt;212&gt; DNA &lt;2213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458  &lt;222&gt; 69233 &lt;222&gt; 69233 &lt;223&gt; Von Heijne matrix</pre>	
<pre> 221&gt; 613</pre>	
<pre> &lt;211&gt; 613 &lt;212&gt; DNA &lt;2213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458  &lt;222&gt; 69233 &lt;222&gt; 69233 &lt;223&gt; Von Heijne matrix</pre>	
<pre> &lt;211&gt; 613 &lt;212&gt; DNA &lt;2213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 69458  &lt;222&gt; 69233 &lt;222&gt; 69233 &lt;223&gt; Von Heijne matrix</pre>	
<pre>4211&gt; 613 4212&gt; DNA 4213&gt; Homo sapiens 4220&gt; 4221&gt; CDS 4222&gt; 69458 4222&gt; 69233 4223&gt; Von Heijne matrix</pre>	60
<pre>4211&gt; 613 4212&gt; DNA 4213&gt; Homo sapiens 4220&gt; 4221&gt; CDS 4222&gt; 69458 4221&gt; sig_peptide 4222&gt; 69233 4223&gt; Von Heijne matrix</pre>	60
<pre>4211&gt; 613 4212&gt; DNA 4213&gt; Homo sapiens 4220&gt; 4221&gt; CDS 4222&gt; 69458  4221&gt; sig_peptide 4222&gt; 69233 4223&gt; Von Heijne matrix</pre>	60 110
<pre>4211&gt; 613 4212&gt; DNA 4213&gt; Homo sapiens 4220&gt; 4221&gt; CDS 4221&gt; Sig_peptide 4222&gt; 69458 4223&gt; Von Heijne matrix</pre>	
<pre>4211&gt; 613 4212&gt; DNA 4213&gt; Homo sapiens  4220&gt; 4221&gt; CDS 4222&gt; 69458  4221&gt; sig_peptide 4222&gt; 69233 4223&gt; Von Heijne matrix 4</pre>	
<pre>4211&gt; 613 4212&gt; DNA 4213&gt; Homo sapiens 4220&gt; 4221&gt; CDS 4221&gt; Sig_peptide 4222&gt; 69458 4223&gt; Von Heijne matrix</pre>	

•	
-40 -35 -30	
ggc cgg gas byg act gag gcc aac cgc ttc gcc tat gct gcc ctc	tgt 206
Gly Arg Xaa Xaa Thr Glu Ala Asn Arg Phe Ala Tyr Ala Ala Leu	·Cys
-25 -20 -15	-10 ttc 254
ggc atc tcc ctg tcc cag tta ttt cct gaa ccc gaa cac agc tcc Gly Ile Ser Leu Ser Gln Leu Phe Pro Glu Pro Glu His Ser Ser	• • •
-5 1 5	
tgc aca gag ttc atg gca ggc ctg gtg ckm tgg ctg gag ttg tct	gaa 302
Cys Thr Glu Phe Met Ala Gly Leu Val Xaa Trp Leu Glu Leu Ser	Glu
10 15 20	gaa 350
gct gtc ttg cca acc atg act gct ttt gcg agc ggc ctg gga ggt Ala Val Leu Pro Thr Met Thr Ala Phe Ala Ser Gly Leu Gly Gly	Glu
25 30 35	
gga sca vma tot ott tot toa aat ttt act gaa gga ccc cat ctt	gaa 398
Gly Xaa Xaa Cys Val Cys Ser Asn Phe Thr Glu Gly Pro His Leu	Glu
40 45 50	55
gga cga ccc gac ggt gat cac tca gga cct tct gag ctt ctc act	caa 446
Gly Arg Pro Asp Gly Asp His Ser Gly Pro Ser Glu Leu Leu Thr	
60 65 70 gga tgg gca cta tgacscccgg gccagagtcc tcgtttgcca catgacctcc	498
Gly Trp Ala Leu	
75	
ctgctccaag tgcccttgga ggagctggat gtccttgaaa agatgttcct ggag	gageetg 558 la 613
aaggaaatca aagaagaga atctgaaatg gccgaggcat cccraaaaaa aaaa	ld 613
<210> 350	
<211> 986	•
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS	
<222> 12638	
<221> sig_peptide	
<222> 12263	•
<pre>&lt;223&gt; Von Heijne matrix score 4.19999980926514</pre>	
seq ITMLQMLALLGYG/LF	
504 2128	
<221> polyA_signal	
<222> 951956	
<221> polyA_site <222> 975985	
₹2227 973903	
<400> 350	
accetateaa g atg gte aac tte eec cag aaa att gea ggt gaa e	tc tat 50
Met Val Asn Phe Pro Gln Lys Ile Ala Gly Glu L	eu Tyr
-80 -75	t ggg 98
gga cct ctc atg ctg gtc ttc act ctg gtt gct atc cta ctc ca Gly Pro Leu Met Leu Val Phe Thr Leu Val Ala Ile Leu Leu Hi	~ 555
-70 -65 -60	<b>-</b>
atg aag acg tot gac act att atc cgg gag ggc acc ctg atg gg	c aca 146
Met Lys Thr Ser Asp Thr Ile Ile Arg Glu Gly Thr Leu Met Gl	y Thr
-55 -50 -45	-40
gee att gge ace tge tte gge tae tgg etg gga gte tea tee tt	c att 194
Ala Ile Gly Thr Cys Phe Gly Tyr Trp Leu Gly Val Ser Ser Ph	5
-35 -30 -2 tac ttc ctt gcc tac ctg tgc aac gcc cag atc acc atg ctg ca	
	qatq 242

Tyr	Phe	Leu		Tyr	Leu	Cys	Asn		Gln	Ile	Thr	Met		Gln	Met	
_	_	-	_						ggg Gly							290
							-	_	ctc Leu						-	338
									atg Met 35							386
									ctc Leu							434
			Met						ctg Leu							482
_	_	_			_	_		_	gag Glu					_		, 530
	-		_		-	_			gcc Ala	_			_	_		578
				_			_		gcc Ala 115		-	_		_		626
_	cag Gln			tga	cccc	acc 1	tgaaa	attc	tt g	gcca	gtcci	ct:	ttcc	cgca		678
ttt tga aaa ccc	gcago aaggo tggg	ctg ( cac a tca g	ccac aagg gctc	tgag ccaa cttt	ct g ga a ga g	tago ctcc aacc	tgcg1 tggc0 cctc0	t aag	gtace gacte acct	ctcc gcaa accc	ttga ggci ctta	atgc tctg cctt	ctg cag cct	tcgg ccaa cttt	atgggg cacttc tgcaga atctct ggaaaa	798 858 918

```
<210> 351
<211> 1447
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 282..389

<221> sig_peptide
<222> 282..332
<223> Von Heijne matrix
score 3.5
seq RWWCFHLQAEASA/HP

<221> polyA_signal
<222> 1413..1418

<221> polyA_site
```

<222> 1437..1447

<400> 351
ataataatat ctaaaaagct aaattttaaa taccagcttt acataaatga ttgtkgactc 60
tggtctgtkt ctgacacctt tccagaaaaa agtcaattgt tcaggtacac caaagaggaa 120

gaagagetgt ggaggeeace etetacaaag etttatagaa ettetggate taacteacaa acaagettee agaagagaet agagaeetta ggeeaggaga tgaaggagtt eagtageaaa gteacacetg tecaatteee tgagetttge teacteaget a atg gga tgg caa agg Met Gly Trp Gln Arg -15	180 240 296
tgg tgg tgc ttt cat ctt cag gca gaa gcc tct gcc cat ccc cct caa  Trp Trp Cys Phe His Leu Gln Ala Glu Ala Ser Ala His Pro Pro Gln  -10 -5 1	344
ggg ctg cag gcc caa ttc tca tgc tgc cct tgg gtg ggc atc tgt Gly Leu Gln Ala Gln Phe Ser Cys Cys Pro Trp Val Gly Ile Cys 5 10 15	389
taacaaadga aaacgtctgg gtggcggcag casctttgct ctgagtgcct acaaagctaa	449
tgcttggtgc tagaaacatc atcattatta aacttcagaa aagcagcagc catgttcagt	509
caggeteatg etgeeteact gettaagtge etgeaggage egeetgeeaa reteceette	569
ctacacctgg cacactgggg tetgcacaag getttgtcaa ccaaaracag ettececeww	629 689
ttgattgcct gtagactttg gagccaaraa acactctgtg tgactctaca cacacttcag	689 749
gtggtttgtg cttcaaagtc attgatgcaa cttgaaagga aacagtttaa tggtggaaat	809
gaactaccat trataactic tgttttttta ttgagaaaat gattcacgaa kkccaaatca	869
gattgccagg aagaaatagg acgtgacggt actgggccct gtgattctcc cagcccttgc	929
agtccgctag gtgagaggaa aagctcttta cttccgccc tggcagggac ttctgggtta	989
tgggagaaac cagagatggg aatgaggaaa atatgaacta cagcagaagc ccctgggcag ctgtgatgga gcccctgaca ttactcttct tgcatctgtc ctgccttctt tccctctgcg	1049
aggcagtggg gtgggattca gagtgcttag tctgctcact gggagaagaa gagttcctgc	1109
gcatgcaagc cctgctgtgt ggctgtcgtt tacatttggg aggtgtcctg tatgtctgta	1169
cgttggggac tgcctgtatt tggaagattt aaaaacctag catcctgttc tcaccctcta	1229
agetgeattg agaaatgact egtetetgta titgtattaa geettaacae tittettaag	1289
tgcattcggt gccaacattt tttagagctg taccaaaaca aaaagcctgt actcacatca	1349
camtgtcatt ttgataggag cgttttgtta tttttacaag gcagaatggg gtgtaacagt	1409
tgaattaaac ttagcaatca cgtgctcaaa aaaaaaaa	1447
<pre>&lt;210&gt; 352 &lt;211&gt; 1641 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; 208339  &lt;221&gt; sig_peptide &lt;222&gt; 208294 &lt;223&gt; Von Heijne matrix</pre>	
<400> 352 agaaccgtga tgggaagatg gacaaggaag agaccaaaga ctggatcctt ccctcagact	60
atgatcatgc agaggcagaa gccaggcacc tggtctatga atcagaccaa aacaaggatg	120
gcaagcttac caaggaggag atcgttgaca agtatgactt atttgttggc agccaggcca cagattttgg ggaggcctta gtacggc atg atg agt tct gag cta cgg agg aac Met Met Ser Ser Glu Leu Arg Arg Asn -25	180 234
cct cat ttc ctc aaa agt aat tta ttt tta cag ctt ctg gtt tca cat Pro His Phe Leu Lys Ser Asn Leu Phe Leu Gln Leu Leu Val Ser His	282
-20 -15 -10 -5	200
gaa att gtt tgc gct act gag act gtt act aca aac ttt tta aga cat Glu Ile Val Cys Ala Thr Glu Thr Val Thr Thr Asn Phe Leu Arg His	330

1 5 10	
gaa aag gcg taatgaaaac catcccgtcc ccattcctcc tcctctctga	379
Glu Lys Ala	•
15	
gggactggag ggaagccgtg cttctgagga acaactctaa ttagtacact tgtg	tttgta 439
ratttacacw wtgtattatg tattaacatg gcgtgtttat ttttgtattt ttcto	ctggtt 499
gggagtatka tatgaaggat caarateete aaeteacaca tgtaracaaa catta	asctct 559
ttactctttc tcaacccctt wtatgatttt aataattctc acttaactaa tttt	gtaagc 619
ctgagatcaa taagaaatgt tcaggagaga ggaaagaaaa aaaatatatg ctcc	acaatt 679
tatatttaga gagagaacac ttagtcttgc ctgtcaaaaa gtccaacatt tcata	
taggggccac atattacatt cagttgctat aggtccagca actgaacctg ccat	tacctg 799
ggcaaggaaa gatccctttg ctctaggaaa gcttggccca aattgatttt cttc	
cccctgtagg actgactgtt ggctaatttt gtcaagcaca gctgtggtgg gaaga	agttag 919
ggccagtgtc ttgaaaatca atcaagtagt gaatgtgatc tctttgcara gcta	tagata 979
gaaacagctg gaaaactaaa ggaaaaatac aagtgttttc ggggcataca tttt	ttttct 1039
gggtgtgcat ctgttgaaat gctcaagact taattatttg ccttttgaaa tcac	tgtaaa 1099
tgcccccatc cggttcctct tcttcccarg tgtgccaagg aattaatctt ggtt	tcacta 1159
caattaaaat teacteettt eeaateatgt eattgaaagt geetttaaeg aaaga	aaatgg 1219
tcactgaatg ggaattetet taagaaacee tgagattaaa aaaagaetat ttgga	ataact 1279
tataggaaag cctagaacct cccagtagag tggggatttt tttcttcttc cctt	tctctt 1339
ttggacaata gttaaattag cagtattagt tatgagtttg gttgcagtgt totta	atcttg 1399
tgggctgatt tccaaaaacc acatgctgct gaatttacca gggatcctca tacc	
tgcaaaccac ttactaccag gcctttttct gtgtccactg gagagettga getca	acactc 1519
aaagatcaga ggacctacag agagggctct ttggtttgag gaccatggct tacc	tttcct 1579
geetttgace cateacacee cattteetee tettteeete teecegetge caaaa	aaaaaa 1639
aa	1641
<210> 353	
<211> 884	
<212> DNA	
<213> Homo sapiens	
.000	
<220>	
<221> CDS	
<222> 69557	
4001 sig montide	
<221> sig_peptide <222> 69224	
<223> Von Heijne matrix	
score 4.69999980926514	
seg LGLALGRLEGGSA/RH	
bed population with	
<221> polyA_signal	
<222> 849854	
<221> polyA_site	
<222> 870883	
<400> 353	
attggctccg gatcgtgcgt gaggcggctt cgtgggcagc gagagtcaca gaca	agacag 60
caagcagg atg gag cac tac cgg aaa gct ggc tct gta gag ctc cc	
Met Glu His Tyr Arg Lys Ala Gly Ser Val Glu Leu Pro	
-50 -45 -40	
cct tcc cca atg ccc cag cta cct cct gat acc ctt gag atg cgg	gtc 158
Pro Ser Pro Met Pro Gln Leu Pro Pro Asp Thr Leu Glu Met Arg	
-35 -30 -25	
cga gat ggc agc aaa att cgc aac ctg ctg ggg ttg gct ctg ggt	
Arg Asp Gly Ser Lys Ile Arg Asn Leu Leu Gly Leu Ala Leu Gly	
-20 -15 -10	-
tta and ago ago not got ago ont gto ato the ter ago	200 254

Tan Oly Oly Oly Oly O all a with tral to large on the column	
Leu Glu Gly Gly Ser Ala Arg His Val Val Phe Ser Gly Ser Gly Arg -5 1 10	
gct gca gga aag gct gtc agc tgc gct gag att gtc aag cgg cgg gtc	302
Ala Ala Gly Lys Ala Val Ser Cys Ala Glu Ile Val Lys Arg Arg Val	
15 20 25	
ccg ggc ctg cac cag ctc acc aag cta ckt ttc ctt caa act gag gac	350
Pro Gly Leu His Gln Leu Thr Lys Leu Xaa Phe Leu Gln Thr Glu Asp 30 35 40	
age tgg gte eca see tea cet gae aca ggg eta rae ece ete aca gtg	398
Ser Trp Val Pro Xaa Ser Pro Asp Thr Gly Leu Xaa Pro Leu Thr Val	
45 50 55	
cgc cgc cat gtg cct gca ktg tgg gtg ctg ctc asc cgg gac ccc ctg	446
Arg Arg His Val Pro Ala Xaa Trp Val Leu Leu Xaa Arg Asp Pro Leu 60 65 70	
gac ccc aat gag tgt ggt tac caa ccc cca gga gca ccc cct ggc ctg	494
Asp Pro Asn Glu Cys Gly Tyr Gln Pro Pro Gly Ala Pro Pro Gly Leu	
75 80 85 90	
ggt too atg coc ago too ago tgt ggc cot cgt too cra aaa agg gct	542
Gly Ser Met Pro Ser Ser Ser Cys Gly Pro Arg Ser Xaa Lys Arg Ala	
95 100 105	
cra rac acc cga tcg tgaaaacctg ctgasccagc ctgttctccg ggcctraatg Xaa Xaa Thr Arg Ser	597
110	
totggggtgc ttgtgccttt totranaagc gttgtgaskg ctcaacatcc ccatcaaggt	657
ttgagtccac aaaagtggac ctccctatca tgcttcccct tccctctagc atgtgggaag	717
ggactgctgt gaagaatgac agatgtgggg cctctgccaa gttctgcatt gctaaataag	777
ggcttcctct gccttctacc tacagtgcat ttgaactgcc ttctgaaaga ggtccakgga	837
gggatttagg aaataaagtt tctacctatt tgaaaaaaaa aaaacac	884
<210> 354	
<211> 729	
<212> DNA <213> Homo sapiens	
(213) Homo sapiens	
<220>	
<221> CDS	
<222> 134325	
<221> sig_peptide <222> 134274	
<pre>&lt;222&gt; 134274 &lt;223&gt; Von Heijne matrix</pre>	
score 5.9000009536743	
seq TWLGLLSFQNLHC/FP	
<221> polyA_site	
<222> 718729	
<400> 354	
atcattttct tatccctgct gatttcaaac cttcccatgg tttagaagca taacctgtaa	60
tgtaatgcaa gtcccctaac tccctggttg ctaacattaa cttccttaag taataatcaa	120
tgaaagavat tot atg cat ggt ttt gaa ata ata too ttg aaa gag gaa	169
Met His Gly Phe Glu Ile Ile Ser Leu Lys Glu Glu	
-45 -40	
tca cca tta gga aag gtg agt cag ggt cct ttg ttt aat gtg act agt Ser Pro Leu Gly Lys Val Ser Gln Gly Pro Leu Phe Asn Val Thr Ser	217
-35 -30 -25 -20	
ggc tca tca tca cca gtg acc tgg ttg ggc cta ctc tcc ttc cag aac	265
Gly Ser Ser Pro Val Thr Trp Leu Gly Leu Leu Ser Phe Gln Asn	203

-15 -10 -5 ctg cat tgc ttc cca gac ctc ccc act gag atg cct cta ara gcc aaa 313

WO 99/31236 -270- PCT/IB98/02122

• •															
Leu H	His Cys	Phe 1	Pro A	Asp :	Leu	Pro 5	Thr	Glu	Met	Pro	Leu 10	Xaa	Ala	Lys	
Gly X	ktc aac Kaa Asn LS		tgago	ccta	gg 9	tggg	ctac	a ac	aaaa	ratt	cta	attt	acc		365
ttgct attta ascaa ttttt tcatt	ctcatc : attgta : atcttt : gaaaa : ctaact :	ttgta tttct aatgg tttat	taaso gttca gaatt aaaca	ta a cg t ga a tg	aaaa gtgt ccgg cctt	catt ttgt atag	tat gat wwa cța	tttt aaaa cagg ittga	gtt cct caa ara	gaat taaa agwt cato	craa ttco ataa tgat	ac a gc a at a	atto agca agcta tttc	catgt itcagt icaaca ictgga	485 545 605 665
															•
<212>	1013	` sapie	ns							,		•			•
<220>		•		•				•	'						
<221> <222>	> CDS > 787	31	-					-	ı		•		,		
<222>	sig_po 782 Von Ho score seq R'	27 eijne 5.09	mat: 9999!	9046		,									
	polyA 1002.	_													
	> 355 ccaag ( ctattt (		ct at	tg c	at c	at	gc c	ctc a Leu I	ca	ca c	tg t	ta d	ctt c Seu C	gt	60 110
	at gag Kis Glu	Gln													158
	aat tta Asn Leu	aat Asn	gca (				Tyr	gga				Leu	ata		206
	gta tgt Val Cys														254
Asn I	-5 att gat Ile Asp														302
10 tat g	gct gtt	tct		15 cqt	cat	aat	gta	att	20 tqc	caq	tta	ctt	tct	25 gac	350
	Ala Val	Ser													
	aaa raa Lys Xaa														398
	caa gac Gln Asp 60	tta					gag					agg			446
gga a Gly s	agt gaa					gag					gaa				494

aat arg ggt ggt gat aga aag gtt gaa raa raa atg aar aag cac gga Asn Xaa Gly Gly Asp Arg Lys Val Glu Xaa Xaa Met Lys Lys His Gly	542
90 95 100 105 agt wct cat atg gga ttc cca raa aac ctg mct aac ggt gcc act gct Ser Xaa His Met Gly Phe Pro Xaa Asn Leu Xaa Asn Gly Ala Thr Ala 110 115 120	590
gac aat ggt gat gat gga tta att ccm cca rgg aaa asc ara aca cct Asp Asn Gly Asp Asp Gly Leu Ile Pro Pro Xaa Lys Xaa Xaa Thr Pro 125 130 135	638
gaa agc cas caa ttt cct gac act gag aat gaa cag tat cac agg gac Glu Ser Xaa Gln Phe Pro Asp Thr Glu Asn Glu Gln Tyr His Arg Asp 140 145 150	686
The Ser Gly His Pro Xaa Phe Pro Thr Thr Leu Pro Ile Lys Gln 155 160 165	731
tgatgaacaa aatgatactc hsaagcmmct ttctgaagam caraacactg gaatattaca	791
agatgagatt ctgattcatg aagaaaagca gatagaagtg gctgaaaatg aattctgagc	851 911
tttctcttag ttataaraaa gaaaaagacc tcttgcatga aaatagtacg ttgcaggaag aaattgtcat gctaaractg gaactagack taatgaaaca tcagagccag ctaararaaa	·971
araaatattt ggaggaaatt gaaagtgtgg aaaaaaaaa	1013
<210> 356 <211> 973	
<212> DNA	
<213> Homo sapiens	
<220>	
<221> CDS <222> 46693	
<221> sig_peptide	
<222> 4690	
<223> Von Heijne matrix score 7.59999990463257 seq CVLVLAAAAGAVA/VF	
<221> polyA_signal	
<222> 937942	
<221> polyA_site <222> 962973	
<pre>&lt;400&gt; 356 aagcggctgg tccccggaag ttggacgcat gcgccgtttc tctgc atg gtg tgc gtt</pre>	57
ctc gtt cta gct gcg gcc gca gga gct gtg gcg gtt ttc cta atc ctg	105
Leu Val Leu Ala Ala Ala Gly Ala Val Ala Val Phe Leu Ile Leu -10 -5 1 5	
cga ata tgg gta gtg ctt cgt tcc atg gac gtt acg ccc cgg gag tct	153
Arg Ile Trp Val Val Leu Arg Ser Met Asp Val Thr Pro Arg Glu Ser	
ctc agt atc ttg gta gtg gct ggg tcc ggt ggg cat acc act gag atc Leu Ser Ile Leu Val Val Ala Gly Ser Gly Gly His Thr Thr Glu Ile	201
25 30 35 ctg agg ctg ctt ggg agc ttg tcc aat gcc tac tca cct aga cat tat	249
Leu Arg Leu Leu Gly Ser Leu Ser Asn Ala Tyr Ser Pro Arg His Tyr  40  45  50	
gtc att gct gac act gat gaa atg agt gcc aat aaa ata aat tct ttt	297
Val Ile Ala Asp Thr Asp Glu Met Ser Ala Asn Lys Ile Asn Ser Phe	

WO 99/31236 -272 - PCT/IB98/02122 -

!	55					60					65					
gaa d Glu 1 70															tac Tyr 85	345
tac a					сса					gtt					ccc	393
tcc a		Val		acc					atg					ccc		441
att (	cac His	agg Arg 120	Val	aag Lys	cca Pro	rat Xaa	ttg Leu 125	gtg Val	ttg Leu	tgt Cys	aac Asn	gga Gly 130	cca Pro	gga Gly	aca Thr	489
tgt ( .Cys \																537
aag a Lys 1 150																<b>585</b>
tta t Leu s																633
gtt ( Val (	cag Gln	tgg Trp	ccg Pro 185	gct Ala	ctg Leu	aaa Lys	gaa Glu	aag Lys 190	tat Tyr	ccc Pro	aaa Lys	tcg Ser	gtg Val 195	tac Tyr	ctt Leu	681
ggg (	Arg			tgac	aaat	gg c	aact	gact	t ct	ttag	aatt	ttg	cast	taa		733
cagta	arta	tg t	acto	aaat	t gg	19999	jaaaa	aaa	ccct	aca	tgtt	tctt	gt a	aagg	cgtct	793
gacag	gtcc	tg a	raat	tatt	gat	ggta	agga	ata	aaaa	atg	twca	gatr	ac t	cagt	gaara	853
															tgcct	913
			iattt	CCCC	t et	arat	aaaa	ata	itgta	itta	ctac	ctgo	aa a	aaaa	aaaaa	973
<210:																
<2112																
<213			apie	ns												,
<220:		_														
<221:			27													
<221: <222:				le												
<223:				mat	rix											
	sc	ore	3.90	0000 FYAG	0953		ı									
<221:				al												
		. •														

<400> 357

<221> polyA\_site <222> 856..867

actggaagaa ctcgtcatgc tctttgtagc gtggtgcttc tgttgctcac aggacaactt 60 gcctttgatg attttcaaga gagttgtgct atgatgtgc aaagtatgca ggaagcaggc 120 ggtca atg cct ctg gga gca agg atc ctt ttc cac ggt gtg ttc tat gcc 170 Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala

-10 -5

Gly Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg	
<u> </u>	66
gca cag gaa gct ctg ggc cct cct ctc aac atc cat tat ctc aag ctc Ala Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu 30 35 40	14
atc gac agg gaa aac ttc gtg gac att gtt rat gcc aag ttg aaa att Ile Asp Arg Glu Asn Phe Val Asp Ile Val Xaa Ala Lys Leu Lys Ile 45 50 55 60	62
cct gtc tct gga tcc aaa tca gag ggc ctt ctc tac gtc cac tca tcc  Pro Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser  65 70 75	10
aga ggt ggc ccc ttt cag agg tgg cac ctt gac gag gtc ttt tta gag Arg Gly Gly Pro Phe Gln Arg Trp His Leu Asp Glu Val Phe Leu Glu 80 85 90	58
ctc aag gat ggt cag cag att cct gtg ttc aag ctc agt ggg gaa aac  Leu Lys Asp Gly Gln Gln Ile Pro Val Phe Lys Leu Ser Gly Glu Asn  95 100 105	06
ggt gat gaa gtg aaa aag gag tagagacgac ccagaagacc cagcttgctt 5 Gly Asp Glu Val Lys Lys Glu 110 115	557
acagacactc ctgcaaccca gktttccagc caccagtggg atgatggtat gtgccagcac 6 atggtaattt tggtgtaatt ctaacttggg cacaacgaat gctatttgtc atttttaaac 7 tgaatccgaa agaaactcct attataaatt taagataatg taatgtattt gaaagtgctt 7 tgtataaaaa agcacatgat aaaaggaatc agaattaata aaatgtttgt tgatctttaa 8	517 577 737 797 857

<210> 358
<211> 519
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 66..320

<221> sig\_peptide
<222> 66..113
<223> Von Heijne matrix
score 3.5
seq TALAAXTWLGVWG/VR

<221> polyA\_signal <222> 490..495

<221> polyA\_site <222> 508..519

<400> 358

aattagegeg taacgeasag actgettget geggeagaga egecagakgt geageteeag
cagea atg gea gtg aeg geg ttg geg geg mrg aeg ttg ett gge gtg ttg
Met Ala Val Thr Ala Leu Ala Ala Xaa Thr Trp Leu Gly Val Trp
-15
-10
-5
gge gtg agg acc atg caa gee ega gge tte gge teg gat eag tee gag
Gly Val Arg Thr Met Gln Ala Arg Gly Phe Gly Ser Asp Gln Ser Glu
1
1
1
1
1
1
1
1
1
1
1
60
110
110
110

WO 99/31236 -274 - PCT/IB98/02122 -

			cgg Arg													206
			gag Glu 35	cag					cga					cag		254
			ctg Leu					aaa					gar			302
		aga	gaa Glu			tgag		tg c	agaa	agaa	aa tt		gcca	ı		350
ggca	caga catg	tc a		ccac	t to	tgtg	gtaaa	cat	ggtt	ctg	gttt	aact	aa t		agaat gtctg	410 470 519
<211 <212	)> 35 l> 10 l> DN l> Ho	28 IA	apie	ns				•		,	٠	•				
	> CI	)S 394	. 8										•			
<222	2> 73	315	eptic 59 eijne	•	rix		•	•		,		,		,		
			4.40 LHLV				3									
		-	_site					•		i						
agct		ag g	c at	g ca	at go	ga tt	eu Le	it ca eu Hi	at ta	ac ct	t tt	ic ca ne Hi	at ac is Th	g ag	gaatgt ga aac g Asn	60 111
cac	acc	ttc	att	atc	cta	cac		25 atc	tta	саа	aaa		20 att	tat	act	159
His	Thr -15	Phe	Ile	Val	Leu	His -10	Leu	Val	Leu	Gln	Gly -5	Met	Val	Tyr	Thr	
			tgg Trp													207
ttg			ctt Leu	ctt												255
			20					25					30	222	993	303
			ctg Leu													303
			tta Leu													351
	aaa		gtg Val			tct					agg					399
tcc			tgc Cys		gtg					gtg					cat	447

																		405	
c	ac	tat	att	taa	gtg	aac	aac	tgc	atc	ggg	gcc	tgg	aac	atc	agg	tmc		495	
н	is	Cvs	Val	Trp	Val	Asn	Asn	Cys	Ile	Gly	Ala	Trp	Asn	110	Arg	Xaa			
				100					105					TIU				E 4 3	
+	tc	ctc	atc	tac	gtc	ttg	acc	ttg	acg	gcc	tcg	gct	gcc	acc	gtc	gcc		543	
D.	he	Leu	Ile	Tvr	Val	Leu	Thr	Leu	Thr	Ala	Ser	Ala	Ala	Thr	Val	Ala			
			115					120					123					-01	
a	++	ata		acc	act	ttt	ctg	gtc	cac	ttg	gtg	gtg	atg	tca	gat	tta		591	
т	10	Val	Ser	Thr	Thr	Phe	Leu	Val	His	Leu	Val	Val	Met	Ser	Asp	Leu			
		130					135					140						·	
+	a.c		gag	act	tac	atc	qat	gac	ctt	gga	cac	ctc	cat	gtt	atg	gac		639	
T	vr	Gln	Glu	Thr	Tyr	Ile	Asp	Asp	Leu	Gly	His	Leu	His	Val	Met	ASP			
-	4 =					150					155					100			
_	~~	atc	ttt	.ctt	att	caq	tac	ctg	ttc	ctg	act	ttt	cca	cgg	att	gtc		687	
П	'h~	Val	Dhe	Leu	Ile	Gln	Tyr	Leu	Phe	Leu	Thr	Phe	Pro	Arg	116	Val			
					165					170					1/5				
٠,	+ ~	ato	cta	ggc	ttt	atc	ata	qtt	ctg	arc	ttc	ctc	ctg	ggt	ggc	tac		735	
τ.	ha	Met	Len	Glv	Phe	Val	Val	Val	Leu	Xaa	Phe	Leu	Leu	Gly	Gly	Tyr			
				700					185					720					
_	·+~	tta	+++	atc	cta	tat	ctq	gcg	gcc	acc	aac	cag	act	act	aac	gag	•	783	
, T	.cy	T.en	Dhe	Val	Leu	Tvr	Leu	Ala	Ala	Thr	Asn	Gln	Thr	Thr	Asn	Glu			
			105					200					205						
	- ~~	tac	242	rat	gac	taa	qcc	tgg	tgc	cag	cgt	tgt	ccc	ctt	gtg	gcc Ala		831	
	-yy	Tvr	Aro	Xaa	Asp	Trp	Ala	Trp	Cys	Gln	Arg	Cys	Pro	Leu	. Val	Ala			
		210					215					220	,						
4	- ~~	act	000	i tca	gca	gar	ccc	caa	gto	cac	cgg	aac	att	cac	tcc	cat		879	
·	ryy	Dro	Pro	Ser	Ala	Glu	Pro	Gln	Val	His	Arg	Asr	ı Ile	His	Ser	111.5			
	225					230					235	)				240			
		++	cac	arc	aac	ctt	caa	gar	ato	: ttt	cta	cct	gcc	: ttt	: cca	tgt		927	
- 3	232 217	7 T.e1	Arc	, La	Asr	Lev	Gln	Glu	ılle	Phe	Lev	Pro	) Ala	Phe	FIC	, cys		•	
					245	,				250	)				232	•			
	cat	. cac	. 200	3 220	g aaa	caa	qaa	tga	cmag	gtgt	atga	actgo	ct t	tgag	gctgt	a		978	
	uic	. gas	) Arc	i Tive	Lys	Glr	Glu	1											
	1175	, 610		260															
	a++		1+++	attt	acad	at	itaas	tcct	c gt	tttt	caaa	aaa	aaaa	aaaa				1028	
	900	بدددر	,	2000			-رد.	-	-										

<210> 360

<211> 452

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 69..434

<221> sig\_peptide

<222> 69..236

<223> Von Heijne matrix score 4.90000009536743 seq FACVPGASPTTLA/FP

<221> polyA\_signal

<222> 419..424

<221> polyA\_site

<222> 441..452

<400> 360

acagcgtgas tcgcccgcca gaagaatatg aaaaagcaga gcganctcgg ttaagggaaa gegeegag atg aeg gge ttt etg etg eeg eec gea age aga ggg aet egg Met Thr Gly Phe Leu Leu Pro Pro Ala Ser Arg Gly Thr Arg

60

110

- <del>5</del> '5	-50	-45	
aga toa tgc agc aga agc ag	a aaa agg caa acg	aga aga agg agg aac	158
Arg Ser Cys Ser Arg Ser Ar -40	-35	-30	
cca agt agc ttt gtg gct to Pro Ser Ser Phe Val Ala Se	g tgt cca acc ctc er Cys Pro Thr Leu	Leu Pro Phe Ala Cys	206
-25 -2 gtg cct gga gcc agt ccc ac	20	-15	254
Val Pro Gly Ala Ser Pro Th	nr Thr Leu Ala Phe	Pro Pro Val Xaa Leu	
-10 -5 aca ggt ccc avc acc gat gg	nc att ccc ttt gcc	5 ctr nak tct qca qcq	302
Thr Gly Pro Xaa Thr Asp Gl	ly Ile Pro Phe Ala	Leu Xaa Ser Ala Ala 20	
ggt ccc ttt tgt gct tcc tt	c ccc tca ggt avc	ctc tct ccc cct ggg	350
Gly Pro Phe Cys Ala Ser Ph 25	ne Pro Ser Gly Xaa 30	Leu Ser Pro Pro Gly	•
cca ctc ccg ggg gtg agg gg	gg tta ccc ctt ccc	agt gtt ttt tat tcc	398
Pro Leu Pro Gly Val Arg Gl		50 Ser val Phe Tyr Ser	
tgt ggg gct cac ccc aaa gt	ta tta aaa gta gct	ttg taattcaaaa	444
Cys Gly Ala His Pro Lys Va	ai Leu Lys vai Ala 65,	Leu	•
aaaaaaa			452
,			
-210: 261			
<210> 361 <211> 875			
<212> DNA		,	
<213> Homo sapiens			
<220>			
<221> CDS <222> 628804	•	•	
<221> sig_peptide <222> 628711			
<223> Von Heijne matrix			
score 4.19999980926 seg LMPVIPALOEAXA/G			
	-		
<221> polyA_site <222> 864875			
		,	
<pre>&lt;400&gt; 361 aaagatggac accgcggagg aag</pre>	acatato tagagtotot	cqqtcaqaag gaacacctga	60
gaaaccgctt tatcatcctt gtg	tatgtac tggcagtatt	aagttngtcc atcaagaatg	120
cttagttcaa tggctgaaac aca			180 240
tgcttttaca ccaatttatt ctc tgctggactg gttacaagta ttg			300
ggcctttgca tggttgggag ttg	ttcctct tacagcatgt	gagtattcat gcctctgatt	360
ggagttattt aaacattgca taa	ctactta atattataaa	gcaatattgc atcatattat	420
tatttgactg atgtttagtt att			480
araaratgtt catcggaact aar			540 600
gaaaraacac agcatacaga atg aaatcaaatc ataattagat atg			654
	Met Leu Xaa I	Leu Ser Arg Ala Thr Lys -25 -20	
rac ggc cgg gcg cgg tgg			702
Xaa Gly Arg Ala Arg Trp I -15	eu Met Pro Val II6 -10	e Pro Ala Leu Gin Giu -5	
gcc gan gca ggc gga tca c	ga ggt cag gag ttt	gaa act agc ctg gcc	750

Ala Xaa Ala Gly Gly Ser Arg Gly Gln Glu Phe Glu Thr Ser Leu Ala	
aac atg gag act gag gca gga gaa ttg ctt aaa ccc agg agg cgg agg Asn Met Glu Thr Glu Ala Gly Glu Leu Leu Lys Pro Arg Arg Arg 15 20 25	798
ttg car tgaactgaga tcgcaccact gcactccagc ttgggcaaca gagcaagact Leu Gln	854
30 ttgtctcgca aaaaaaaaa a	875
· * *	
<210> 362 <211> 531 <212> DNA <213> Homo sapiens	
<220>	
<221> CDS <222> 70366	•
<221> sig_peptide <222> 70108	
<223> Von Heijne matrix score 3.5	
seq MHLLSNWANPASS/RR	
<221> polyA_signal <222> 496501	
<221> polyA_site <222> 521531	
<400> 362	60
aagtggccat ggcggataca gcgactacag catcggcggc ggcggctagt gccgctagcg cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg -10 -5	111
cgt cct tct atg gcc gct tca ggc act tct tgg ata tca tcg acc ctc Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu 5 10 15	159
gca cac tct ttg tca ctg aga gac gtc tca gag agg ctg tgc agc tgc Ala His Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys 20 25 30	207
tgg agg act ata agc atg gga ccc tgc gcc cgg ggg tca cca atg aac Trp Arg Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn	255
35 40 45	303
agc tct gga gtg cac aga aaa tca agc agg cta ttc tac atc cgg aca Ser Ser Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr 50 55 60 65	
cca atg aga aga tct tca tgc cat tta gaa tgt crg gtt ata ttc ctt Pro Met Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val Ile Phe Leu 70 75 80	351
ttg gga cgc caa ttg taaktgttac cttcaaagga tttccttttc taaaaaatta Leu Gly Arg Gln Leu 85	406
ttttaratgt ctaactttat gttattgctc acgggtattt gactgaattg ttgatttagg ataagtcaat tcctggaggg aaattaccaa ataaaatgat atgtatttct taccacaaaa aaaaa	466 526 531

```
<210> 363
<211> 1244
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 70..366
<221> sig_peptide
<222> 70..108
<223> Von Heijne matrix
     score 3.5
     seg MHLLSNWANPASS/RR
<221> polyA site
<222> 1233..1244
<400> 363
aagtggccat ggcggataca gcgactacag catcggcggc ggcggctagt gccgctagcg
                                                                       60
cctcgagcg atg cac ctc ctt tcc aac tgg gca aac ccc gct tcc agc aga
                                                                      111
          Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg
                                          -5
                      -10
                                                                      159
cgt cct tct atg gcc gct tca ggc act tct tgg ata tca tcg acc ctc
Arg Pro Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu
                                10
                                                                      207
gca cac tot tig toa oig aga gad gto toa gag agg oig igo ago igo
Ala His Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys
                            25
        20
tgg agg act ata agc atg gga ccc tgc gcc cgg ggg tca cca atg aac
                                                                      255
Trp Arg Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn
                        40
                                            45
                                                                      303
ago tot qqa qtq cac aga aaa toa ago agg ota tto tac ato ogg aca
Ser Ser Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr
                    55
50
cca atg aga aga tct tca tgc cat tta raa tgt cag gtt ata ttc ctt
                                                                      351
Pro Met Arg Arg Ser Ser Cys His Leu Xaa Cys Gln Val Ile Phe Leu
                                    75
                70
            ٠,
                                                                      406
ttg gga cgc caa ttg tagtcggtct tctcttgccc aaccagacac tggcatccac
Leu Gly Arg Gln Leu
            85
                                                                      466
tgtcttctgg cagtggctga accagagcca caatgcctgt gtcaactatg caaaccgcaa
tgcraccaag ccttcacctg catccaagtt catccaggga tacctgggag ctgtcatcag
                                                                      526
                                                                      586
cgccgtctcc attgctgtgg gccttatktc ctggttcaga aagccaacaa gttcacccca
                                                                      646
gccaccegce ttetcateca gaggtttgtg cegtteeetg etgtagecag tgccaatate
                                                                      706
tgcaatgtgg tcctgatgcg gtacggggag ctggaggaag ggattgatgt cctggacagc
                                                                      766
gatggcaacc tegtgggete etccaagate geagecegae aegecetget ggagaeggeg
ctgacgcgag tggtcctgcc catgcccatc ctggtgctac ccccgatcgt catgtccatg
                                                                      826
                                                                      886
ctggagaaga cggctctcct gcaggcacgc ccccggctgc tcctccctgt gcaaagcctc
gtgtgcctgg cagccttcgg cctggccctg ccgctggcca tcagcctctt cccgcaaatg
                                                                      946
                                                                     1006
tcagagattg aaacatccca attagagccg gagatagccc aggccacgag cagccggaca
gtggtgtaca acaaggggtt gtgagtgtgg tcagcggcct ggggacggag cactgtgcag
                                                                     1066
ccggggagct gaggggcarg gccgtagact cacggctgca cctgcaggga gcagcacgcc
                                                                     1126
                                                                     1186
aaccccagca gtcctgggcc ccctgggaga gtgctcaacc tacagtggag ggagactgac
ccattcacat tttaacatag gcaagaggag ttctaacaca tttcgtacaa aaaaaaaa
```

<sup>&</sup>lt;210> 364

<sup>&</sup>lt;211> 631

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Homo sapiens

```
<220>
<221> CDS
<222> 111..434
<221> sig_peptide
<222> 111..185
<223> Von Heijne matrix
     score 3.90000009536743
      seq WIAAVTIAAGTAA/IG
<221> polyA_site
<222> 618..631
<400> 364
aatcgcggag tcggtgcttt agtacgccgc tggcaccttt actctcgccg gccgcggaa
cccgtttgag ctcggtatcc tagtgcacac gccttgcaag cgacggcgcc atg agt
                                                                      116
                                                       Met Ser
ctg act tcc agt tcc agc gta cga gtt gaa tgg atc gca gca gtt acc
                                                                      164
Leu Thr Ser Ser Ser Val Arg Val Glu Trp Ile Ala Ala Val Thr
att gct gct ggg aca gct gca att ggt tat cta gct tac aaa aga ttt
                                                                      212
Ile Ala Ala Gly Thr Ala Ala Ile Gly Tyr Leu Ala Tyr Lys Arg Phe
tat gtt aaa gat cat cga aat aaa gct atg ata aac ctt cac atc cag
                                                                      260
Tyr Val Lys Asp His Arg Asn Lys Ala Met Ile Asn Leu His Ile Gln
                    15
                                        20
                                                                      308
aaa gac aac ccc aag ata gta cat gct ttt gac atg gag gat ttg gga
Lys Asp Asn Pro Lys Ile Val His Ala Phe Asp Met Glu Asp Leu Gly
                30
                                    35
                                                                      356
gat aaa gct gtg tac tgc cgt tgt tgg agg tcc aaa aag ttc cca ttc
Asp Lys Ala Val Tyr Cys Arg Cys Trp Arg Ser Lys Lys Phe Pro Phe
                                50.
                                                                      404
tgt gat ggg gct cac aca aaa cat aac gaa gag act gga gac aat gtg
Cys Asp Gly Ala His Thr Lys His Asn Glu Glu Thr Gly Asp Asn Val
        60
                            65
                                                                      454
ggc cct ctg atc atc aag aaa aaa gaa act taaatggaca cttttgatgc
Gly Pro Leu Ile Ile Lys Lys Lys Glu Thr
tgcaaatcag cttgtcgtga agttacctga ttgtttaatt araatgacta ccacctctgt
                                                                      514
                                                                      574
ctgattcacc ttcgctggat tctaaatgtg gtatattgcm aactgcagct ttcacattta
                                                                      631
tggcatttgt cttgttgaaa catcgtggtg cacatttgtt taaacaaaaa aaaaaaa
```

<210> 365

<211> 781

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 19..567

<221> sig peptide

<222> 19..63

<223> Von Heijne matrix
 score 8.39999961853027
 seq AMWLLCVALAVLA/WG

<221> polyA\_signal

<222> 749..7545 <221> polyA\_site <222> 771..781 <400> 365 aagtgctgct tacccatc atg gaa gca atg tgg ctc ctg tgt gtg gcg ttg 51 Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu -15 -10 99 gcg gtc ttg gca tgg ggc ttc ctc tgg gtt tgg gac tcc tca gaa cga Ala Val Leu Ala Trp Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg 147 atg aag agt cgg gag cag gga aga cgg ctg gga gcc gaa agc cgg acc Met Lys Ser Arg Glu Gln Gly Arg Arg Leu Gly Ala Glu Ser Arg Thr 20 195 ctg ctg gtc ata gcg cac cct gac gat gaa gcc atg ttt ttt gct ccc Leu Leu Val Ile Ala His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro 30 243 aca gtg cta ggc ttg gcc cgc cta agg cac tgg gtg tac ctg ctt tgc Thr Val Leu Gly Leu Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys -50 55 291 ttc tct gca gga aat tac tac aat caa gga gag act cgt aag aaa gaa Phe Ser Ala Gly Asn Tyr Tyr Asn Gln Gly Glu Thr Arg Lys Lys Glu 70 65 ctt ttg car agc tgt gat gtt ttg ggg att cca ctc tcc agt gta atg 339 Leu Leu Gln Ser Cys Asp Val Leu Gly Ile Pro Leu Ser Ser Val Met 90 85 387 att att gac aac agg gat ttc cca rat gac cca ggc atg cag tgg gac Ile Ile Asp Asn Arg Asp Phe Pro Xaa Asp Pro Gly Met Gln Trp Asp 100 105 435 aca rag cac gtg gcc ara gtc ctc ctt cag cac ata gaa gtg aat ggc Thr Xaa His Val Ala Xaa Val Leu Leu Gln His Ile Glu Val Asn Gly 115 120 atc aat ctg gtg gtg act ttc gat gca ggg gga rta agt ggc cac agc 483 Ile Asn Leu Val Val Thr Phe Asp Ala Gly Gly Xaa Ser Gly His Ser 135 130 531 aat cac att gct ctg tat gca gct gtg agg aag ctt gag ggc caa att Asn His Ile Ala Leu Tyr Ala Ala Val Arg Lys Leu Glu Gly Gln Ile 150 577 tgc aag ccc tgt ggc act gga caa gac ttt aag gaa tgagtgctgt Cys Lys Pro Cys Gly Thr Gly Gln Asp Phe Lys Glu 165 160 637 caatcagtgt gcctccacct tcaccatctt cttcccctta ctctcacttc cgtcatgtgt 697 tttatacaac tctcaaatct ttcttggaga aggaggatat acatacataa tatgaaatgt 757 gtttgttctt cacagtcacc cgattttact gatatttatt tgcattttac caataaaaag 781 aaaatgcaag ctcaaaaaaa aaaa

<210> 366
<211> 931
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> 19..312

<221> sig\_peptide
<222> 19..63
<223> Von Heijne matrix

score 8.39999961853027

## seq AMWLLCVALAVLA/WG

<221> polyA\_signal <222> 896..901 <221> polyA site <222> 921..931 <400> 366 51 aagtgctgct tacccatc atg gaa gca atg tgg ctc ctg tgt gtg gcg ttg Met Glu Ala Met Trp Leu Leu Cys Val Ala Leu -15 99 qcg gtc ttg gca tgg ggc ttc ctc tgg gtt tgg gac tcc tca gaa cga Ala Val Leu Ala Trp Gly Phe Leu Trp Val Trp Asp Ser Ser Glu Arg 147 atg aag agt cgg gag cag gga rga cgg ctg gga gcc gaa agc cgg acc Met Lys Ser Arg Glu Gln Gly Xaa Arg Leu Gly Ala Glu Ser Arg Thr 15 ctg ctg gtc ata gcg cac cct gac gat gaa gcc atg ttt ttt gct ccc · 195 Leu Leu Val Ile Ala His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro 35 40 243 aca gtg cta ggc ttg gcc cgc cta agg cac tgg gtg tac ctg ctt tgc Thr Val Leu Gly Leu Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys 50 291 tto tot goa gtt tto ogt agg gag ota agt gaa tac acc gaa rgt ott Phe Ser Ala Val Phe Arg Arg Glu Leu Ser Glu Tyr Thr Glu Xaa Leu 70 65 342 acc tot gaa coc oto ama goo tagggacagg arcggccggc ttacctggtg Thr Ser Glu Pro Leu Xaa Ala 402 ggttggggga cgtcggcagc tcrcgtacta cgccagcagg attganganc acagaaacag ttgchsttgg ttgtattcag tacctkcatt tccgttggga actccaccwg tacttgttat 462 kctgtggaac tttttttat ttgtagaagg agcaagaata ttgaccttac tatatagcac 522 582 acgaaacaat ctatgctgta tcgtgcctgc tcaatcctta aagttaactt ctaatgatag 642 taaaaracct tcctgctgcc tttaaaatgc agcttgtgct aktaacatgc atgtgtcaaa

ttgaaraatt agacatagat gactaratar aaagtaattt tgtaggtaat tttaragttc

aactccaccc agctttcakt gaaggaacct ttcaaataat aratttttgc ttaccatara raaaaratca aatgacaaag caaatattga ccattaagct ggaatatggt gataattgaa

cagitgtata aatgaaktaa ttgaattgta cacatacaat gggtgaattt tatggcatgt

caaagtatac ctcaataaag ctatttttt aaattgcmaa aaaaaaaaa

702 762

822 882

931

<210> 367

<211> 849

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 64..612

<221> sig\_peptide

<222> 64..234

<223> Von Heijne matrix
 score 3.79999995231628
 seq QLWLVMEFCGAGS/VT

<221> polyA\_site <222> 839..849

<400> 367

															tcaag	60
gtt	atg Met	gat Asp	gtc Val -55	aca Thr	GJA aaa	gat Asp	gaa Glu	gag Glu -50	gaa Glu	gaa Glu	atc Ile	aaa Lys	caa Gln -45	gaa Glu	att Ile	108
aac Asn	atg Met	ttg Leu -40	aag Lys	aaa Lys	tat Tyr	tct Ser	cat His -35	cac His	cgg Arg	aat Asn	att	gct Ala -30	aca Thr	tac Tyr	tat Tyr	156
														ctt Leu		204
														atc Ile 5		252
aac														atc Ile		300
														gtg Val		348
														gca Ala		396
														aca Thr		444
ggc														cca Pro 85		492
														aar Lys		540
														Gly 999		588
		Ser	gtg Val						gagc	tct	cttc	ctca	tc c	cccg	gaatc	642
gct tac	cgcc tggt gaga	tcg aaa cca	aaat	caca aatg	gc c	agcg gaca	acca ggtc	g ca	acag	aaca	att	gatg	aag	catc	agagct cattta atagaa	702, 762 822 849

<210> 368

<211> 644

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 39..458

<221> sig\_peptide

<222> 39..80

<223> Von Heijne matrix score 4.40000009536743 seq FLTALLWRGRIPG/RQ

<221> polyA\_signal <222> 613..618

WO 99/31236 -283 - PCT/IB98/02122 -

<221> polyA\_site <222> 633..644"

<400> 368 56 ageggagaeg cagagtettg ageagegegn caggeace atg tte etg act geg etc Met Phe Leu Thr Ala Leu 104 ctc tgg cgc ggc cgc att ccc ggc cgt cag tgg atc ggg aag cac cgg Leu Trp Arg Gly Arg Ile Pro Gly Arg Gln Trp Ile Gly Lys His Arg -5 cgg ccg cgg ttc gtg tcg ttg cgc gcc aag cag aac atg atc cgc cgc 152 Arg Pro Arg Phe Val Ser Leu Arg Ala Lys Gln Asn Met Ile Arg Arg 200 ctq gag atc gag gcg gag aac cat tac tgg ctg agc atg ccc tac atg Leu Glu Ile Glu Ala Glu Asn His Tyr Trp Leu Ser Met Pro Tyr Met 35 25 248 acc cgg gag cag gag cgc ggc cac gcc gcg ttg cgc agg agg gag gcc Thr Arg Glu Gln Glu Arg Gly His Ala Ala Leu Arg Arg Arg Glu Ala 45 ttc gag gcc ata aag gcg gcc gcc act tcc aag ttc ccc ccg cat aga 296 Phe Glu Ala Ile Lys Ala Ala Ala Thr Ser Lys Phe Pro Pro His Arg 70 ttc att gcg gac cag ctc gac cat ctc aat vgt cac caa gaa atg gtc 344 Phe Ile Ala Asp Gln Leu Asp His Leu Asn Xaa His Gln Glu Met Val 80 392 cta atc ctg agt cgt cac cct tgg att tta tgg atc acg gag ctg acc Leu Ile Leu Ser Arg His Pro Trp Ile Leu Trp Ile Thr Glu Leu Thr 100 atc ttt acc tgg tct gga ctg aaa aac tgt agc ttg tgt gaa aat gag 440 Ile Phe Thr Trp Ser Gly Leu Lys Asn Cys Ser Leu Cys Glu Asn Glu 120 115 110 488 ctt tgg acc agt ctt tat taaaacaaac aaacatgagt agtctgcata Leu Trp Thr Ser Leu Tyr 548 togaatatot agagototaa accocccaat acttaaaagt ctaattgctg toctgtggtt 608 tcattagtct gataggaaga tagggatttc ctcagtcaca gatgatattt tgaaggaaag 644 ctgcaataaa gccacaatga tttgaaaaaa aaaaaa

<210> 369

<211> 918

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 9..185

<221> sig\_peptide

<222> 9..50

<223> Von Heijne matrix
 score 3.70000004768372
 seq AALVTVLFTGVRR/LH

<221> polyA\_site <222> 906..918

<400> 369

agctcagc atg gct gct tta gtg act gtt ctc ttc aca ggt gtc cgg agg Met Ala Ala Leu Val Thr Val Leu Phe Thr Gly Val Arg Arg

WO 99/31236 -284- PCT/IB98/02122 -

Leu His Cys Ser Ala Xaa Leu Gly Arg Ala Ala Ser Gly Xaa Tyr Ser  1 10 15	
agg aac tgg ctg cca acc cct ccg gct acg ggc ccc tta ccg agc tcc Arg Asn Trp Leu Pro Thr Pro Pro Ala Thr Gly Pro Leu Pro Ser Ser 20 25 30	146
cag act ggt cat atg cgg atg gcc gcc ctg ctc ccc caa tgaaaggcca Gln Thr Gly His Met Arg Met Ala Ala Leu Leu Pro Gln 35 40 45	195
gettegaaaa aaagetgaaa gggagacktt tgcaaracra kttgtactge tgtcacagga aatggacget ggattacaas catggcaset caggcagcar aakttgcagg aaraacaaag gaagcaggaa aatgetetta aacecaaagg ggetteaetg aaaaseccae ttecaaktea ataaaaagea acteetgeet eeetteete eackkteece atetgtette aragcaaaar agetgggacm eeaaraacaa getgttarat eactgeetgg gaggettgge ttartaetet eatetetggt tecatteeag tteagetaag tettgetta aaatttttae eteetagggggggggg	255 315 375 435 495 555 615 675 735 795 855 918
<210> 370 <211> 472 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 14316	
<221> sig_peptide <222> 14121 <223> Von Heijne matrix score 5.19999980926514 seq PLRLLNLLILIEG/SV	
<221> polyA_signal	
<221> polyA_site   <222> 458471	
<pre>&lt;400&gt; 370 attatataga gcc atg ggg cct tac aac gtg gca gtg cct tca gat gta</pre>	49
tct cat gcc cgc ttt tat ttc tta ttt cat cga cca tta agg ctg tta Ser His Ala Arg Phe Tyr Phe Leu Phe His Arg Pro Leu Arg Leu Leu -20 -15 -10	97
aat ctg ctc atc ctt att gag ggc agt gtc gtc ttc tat cag ctc tat Asn Leu Leu Ile Leu Ile Glu Gly Ser Val Val Phe Tyr Gln Leu Tyr -5 1 5	145
tcc ttg ctg cgg tcg gag aag tgg aac cac aca ctt tcc atg gct ctc Ser Leu Leu Arg Ser Glu Lys Trp Asn His Thr Leu Ser Met Ala Leu 10 15 20	193
atc ctc ttc tgc aac tac tat gtt tta ttt aaa ctt ctc cgg gac aga  Ile Leu Phe Cys Asn Tyr Tyr Val Leu Phe Lys Leu Leu Arg Asp Arg  25 30 35 40	241

WO 99/31236 -285- PCT/IB98/02122

wta kta tta ggc agg gca tac tcc tac cca ctc aac agt tat gaa ctc	
Xaa Xaa Leu Glÿ Arg Ala Tyr Ser Tyr Pro Leu Asn Ser Tyr Glu Leu 45 50 55	
aag gca aac twa gct gcc tct caw caa tgagggagaa ctcagataaa Lys Ala Asn Xaa Ala Ala Ser Xaa Gln	336
aatattttca tacgttctat ttttttcttg tgatttttat aaatatttaa gatatttt atttttgtata ctattatgtt ttgaaagtcg ggaagagtaa gggatattaa atgtatcc aaacaaaaa aaaaam	
<210> 371 <211> 1504 <212> DNA	
<213> Homo sapiens	
<220> <221> CDS <222> 701092	
<221> sig_peptide <222> 70234 <223> Von Heijne matrix score 4.09999990463257 seq AVCAALLASHPTA/EV	
<221> polyA_signal	
<221> polyA_site <222> 14931504	
<400> 371	
agaaatcgta ggacttccga aagcagcggc ggcgtttgct tcactgcttg gaagtgtg tgcgcgaag atg cga aag gtg gtt ttr att acc ggg gct agc agt ggc a	
Met Arg Lys Val Val Leu Ile Thr Gly Ala Ser Ser Gly I	att 111
-55 -50 -45	att 111 Ile
-55 -50 -45  ggc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat  Gly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His  -40 -35 -30	att 111 Ile 159
-55 -50 -45  ggc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat Gly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His	111 Ile 159 s 207
9gc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat cat Gly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His -40 -35 -30 -30  ctg tgt ttg gcg tgc agg aat atg agc aag gca gaa gct gtc tgt gcg Leu Cys Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala -25 -20 -15 -16  gct ctg ctg gcc tct cac ccc act gct gag gtc acc att gtc cag gtg Ala Leu Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val	att 111 Ile 159 s 207 a 255
9gc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat cat gcly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His -40 -35 -35 -30 ctg ttg ttg gcg tgc agg aat atg agc aag gca gaa gct gtc tgt gcg Leu Cys Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala -25 -20 -15 -16 gct ctg ctg gcc tct cac ccc act gct gag gtc acc att gtc cag gtg Ala Leu Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val -5 1	att 111 Ile
9gc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat cat Gly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His -40 -35 -30 -30  ctg tgt ttg gcg tgc agg aat atg agc aag gca gaa gct gtc tgt gcg Leu Cys Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala -25 -20 -15 -16  gct ctg ctg gcc tct cac ccc act gct gag gtc acc att gtc cag gtg Ala Leu Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val	att 111 Ile 159 s 207 a 255 l 303
9gc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat gly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His -40 -35 -30 -30  ctg tgt ttg gcg tgc agg aat atg agc aag gca gct gtc tgt gct Leu Cys Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala -25 -15 -10  gct ctg ctg gcc tct cac ccc act gct gag gtc acc att gtc cag gtg Ala Leu Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val Ser Asp Val Ser Asn Leu Gln Ser Phe Phe Arg Ala Ser Lys Glu Leu Lys 10 15 20  caa agg ttt cag aga tta gac tgt ata tat cta aat gct ggg atc atc	att 111 Ile 159 s 207 a 255 l 303 s 351
9gc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat gcly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His -40	att 111 Ile 159 s 207 a 255 l 303 s 351
ggc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat         Gly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His         -40       -35         ctg tgt ttg gcg tgc agg aat at ggc aag gca gaa gct gtc tgt gct         Leu Cys Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala         -25       -20         gct ctg ctg gcc tct cac ccc act gct gag gtc acc att gtc cag gtg         Ala Leu Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val         Asp Val Ser Asn Leu Gln Ser Phe Phe Arg Ala Ser Lys Glu Leu Lys         10       15         caa agg ttt cag aga tta gac tgt ata tat cta aat gct ggg atc atc         Gln Arg Phe Gln Arg Leu Asp Cys Ile Tyr Leu Asn Ala Gly Ile Met         25       30         35         36         37         38       35         39       35         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40	att 111 Ile 159 s 207 a 255 l 303 s 351 t 399
ggc         ctg         gcc         ctc         tgc         aag         cgg         ctg         ctg         gcg         gcg         gaa         gat         gat         gag         ctt         cat           Gly         Leu         Ala         Leu         Cys         Lys         Arg         Leu         Leu         Ala         Glu         Asp         Asp         Glu         Leu         His           -40         -35         -35         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30         -30	att 111 Ile 159 s 207 a 255 l 303 s 351 t 399
ggc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat         Gly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His         -40       -35         ctg tgt ttg gcg tgc agg aat at ggc aag gca gaa gct gtc tgt gct         Leu Cys Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala         -25       -20         gct ctg ctg gcc tct cac ccc act gct gag gtc acc att gtc cag gtg         Ala Leu Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val         Asp Val Ser Asn Leu Gln Ser Phe Phe Arg Ala Ser Lys Glu Leu Lys         10       15         caa agg ttt cag aga tta gac tgt ata tat cta aat gct ggg atc atc         Gln Arg Phe Gln Arg Leu Asp Cys Ile Tyr Leu Asn Ala Gly Ile Met         25       30         35         36         37         38       35         39       35         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40         40       40	att 111 Ile 159 s 207 a 255 l 303 s 351 t 399 r
ggc ctg gcc ctc tgc aag cgg ctg ctg gcg gaa gat gat gag ctt cat         Gly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His         -40       -35       -35       -30       gca gaa gct gtc gtc gcg       gcg ctg ctg gcc Leu His         Leu Cys Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala       -20       -15       -16       -16         gct ctg ctg gcc tct cac ccc act gct gag gtc aga gtc acc att gtc cag gtc       -16       -16       -16       -16         gat gtc agc aac ctg ctg acc tct cac ccc act gct gag gtc acc att gtc cag gtc       -15       -16       -16       -16         gat gtc agc aac ctg cag tca ttc tc cac ggg gcc tcc aag gaa ctt agc       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16       -16	att 111 Ile 159 s 207 a 255 l 303 s 351 t 399 r 447
-55       -50       -45         ggc ctg gcc ctc tgc aag cgg ctg ctg ctg gcg gaa gat gat gag ctt cat       Gly Leu Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His         -40       -35       -30         ctg tgt ttg gcg tgc agg aat at atg agc aag gca gaa gct gtc tgt gcg       Leu Cys Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala         -25       -20       -15         gct ctg ctg gcc tct cac ccc act gct gag gtc acc att gtc cag gtc       Ala Leu Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val         Ala Leu Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val       -5         gat gtc agc aac ctg cag tca ttc ttc cgg gcc tcc aag gaa ctt aag         Asp Val Ser Asn Leu Gln Ser Phe Phe Arg Ala Ser Lys Glu Leu Lys         10       15         20         caa agg ttt cag aga tta gac tgt ata tat cta aat gct ggg atc atc         Gln Arg Phe Gln Arg Leu Asp Cys Ile Tyr Leu Asn Ala Gly Ile Met         25       30         30       35         cct aat cca caa cta aat atc aaa gca ctt ttc ttc ttc ttc ttc ttt ttc ttt ttc ttt ttc ttt ttc         Pro Asn Pro Gln Leu Asn Ile Lys Ala Leu Phe Phe Gly Leu Phe Set         40       45         aga aaa gtg att cat atg ttc tcc aca gct gaa ggc ctg ctg ctg	att 111 Ile 159 s 207 a 255 l 303 s 351 t 399 r 447 a 495

								cgg Arg								543
His	Ser 105	Asp	Asn	Pro	Ser	Gln 110	Leu	atc Ile	Trp	Thr	Ser 115	Ser	Arg	Ser	Ala	591
Arg 120	Lys	Ser	Asn	Phe	Ser 125	Leu	Glu	gac Asp	Phe	Gln 130	His	Ser	Lys	Gly	Lys 135	639
Glu	Pro	Tyr	Ser	Ser 140	Ser	Lys	Tyr	gcc Ala	Thr 145	Asp	Leu	Leu	Ser	Val 150	Ala	687
								ggt Gly 160								735
								aca Thr								783
								ata Ile								831
								aat Asn								879
								ctc Leu								927
_	_			7-			_	aat Asn 240			_	,	_	_	_	975
-		_	_	_		_	_	aaa Lys				_		_	_	1023
								att Ile								1071
agg Arg 280	ctc Leu	agt Ser	ggc Gly	tca Ser	tgc Cys 285	cta Leu	taat	tcc	agc a	actt	ggg	ag go	ccaa	ggcag	3	1122
															tgtct	
															cagcta gagctg	
															gtata	1362
															acctto	
					aa aa		JLACI	- yaq	Jeeg	yata	atai	_gca1	9	JLAAI	taaact	1482 1504

```
<210> 372
<211> 765
<212> DNA
<213> Homo sapiens
```

<220>

<221> CDS <222> 274..597

## seg LLFDLVCHEFCQS/DD

<221> polyA signal <222> 731..736 <221> polyA\_site <222> 754..765 <400> 372 accaggaaca tccagctatt tatgatagca tttgcttcat tatgtcaagt tcaacaaatg 60 ttgacttgct ggtgaaggtg ggggaggttg tggacaagct ctttgatttg gatgagaaac 120 taatgttaag aatgggtcag aaatggggct gctcagcctc tggaccaacc ccaggaagag 180 totgaagago agcoagtgtt toggottgtg cootgtatac ttgaagotgo caaacaagta 240 294 egttetgaaa atceagaatg gettgatgtt tac atg cac att tta caa etg ett Met His Ile Leu Gln Leu Leu 342 act aca gtg gat gat gga att caa gca att gta cat tgt cct gac act Thr Thr Val Asp Asp Gly Ile Gln Ala Ile Val His Cys Pro Asp Thr -25 -30 gga aaa gac att tgg aat tta ctt ttt gac ctg gtc tgc cat gaa ttc 390 Gly Lys Asp Ile Trp Asn Leu Leu Phe Asp Leu Val Cys His Glu Phe -10 -15 438 tgc cag tct gat gat cca gcc atc att ctt caa raa car aaa acr gtg Cys Gln Ser Asp Asp Pro Ala Ile Ile Leu Gln Xaa Gln Lys Thr Val 486 cta gcc tct gtt ttt tca gtg ttg tct gcc atc tat gcc tca cag act Leu Ala Ser Val Phe Ser Val Leu Ser Ala Ile Tyr Ala Ser Gln Thr 20 534 gag caa gak tat cta aar ata raa aaa gga gac ggt ggc tca ggg agt Glu Gln Xaa Tyr Leu Lys Ile Xaa Lys Gly Asp Gly Gly Ser Gly Ser 40 35 aaa gga agg cca ktt gan caa aca gaa ktg ttc ctc tgc att tca aaa 582 Lys Gly Arg Pro Xaa Xaa Gln Thr Glu Xaa Phe Leu Cys Ile Ser Lys 55 637 cct tct tcc ttt cta tagccctgtg gtggaagatt ttattaaaat cctacgtgaa Pro Ser Ser Phe Leu 65 697 gttgataagg cgcttgctga tgacttggaa aaaaacttcc caagtttgaa ggttcagact 757 taaaacctga attggaatta cttctgtaca agaaataaac tttatttttc tcactgacaa 765

<210> 373

aaaaaaa

<211> 1041

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 230..469

<221> sig\_peptide

<222> 230..307

<223> Von Heijne matrix score 4.90000009536743 seq VLCTNQVLITARA/VP

<221> polyA\_signal

<222> 1004..1009

<221> polyA site

<222> 1027..1040

<400> 373													
aacttccaag ttgtagtgtt gttgttttca gcctgctgct gctgctgcta ttgcggctag													
gggaaccgtc gtggggaagg atggtgtgcg aaaaatgtga aaagaaactt ggtactgtta													
tcactccaga tacatggaaa gatggtgcta ggaataccac agaaagtggt ggaagaaagc													
tgaatgaaaa taaagctttg acttcaaaaa aagccagaat tgatccata atg gaa gaa													
Met Glu Glu													
-25													
ata agt tot coa ott gta gaa ttt gta aaa gtt ttg tgc acc aac cag	286												
Ile Ser Ser Pro Leu Val Glu Phe Val Lys Val Leu Cys Thr Asn Gln													
-20 -15 -10													
gtt ctc att act gcc agg gct gtg cct aca aaa aag gca tct gtg cga	334												
Val Leu Ile Thr Ala Arg Ala Val Pro Thr Lys Lys Ala Ser Val Arg -5 5													
tgt gtg gaa aaa agg ttt tgg ata cca aaa act aca agc aaa cat ctg	382												
Cys Val Glu Lys Arg Phe Trp Ile Pro Lys Thr Thr Ser Lys His Leu	302												
10 15 20 25													
tot aga tgt att gat gga att tot ggo ttt ota aat gat ttt act tto	430												
Ser Arg Cys Ile Asp Gly Ile Ser Gly Phe Leu Asn Asp Phe Thr Phe	150												
30 35 40													
tgc ctt gaa ttt tca agg cat aga tgt caa ctt aca gaa taacatgtkt	479												
Cys Leu Glu Phe Ser Arg His Arg Cys Gln Leu Thr Glu													
45 50													
taagataatt aagtktaaac cagaraattt gattgttact cattttgctc tcatgtkcta	539												
aaacagcaac agtgtaacta gtcttttgtt gtaaatggtt attttcctta taaaaatttt	599												
aaaaactaag tggcaaattc catgaaaata tttctcagtt ctgtatgcac ttttatttaa	659												
cattattcat ataattctcc ccccaccact ttatttat	719												
agataataaa tactttgctc tgaatttggc atccaaagtt aacatttctc ccctcactcc	779												
cttgctggtg tcatagttat tagaatcagc agcctcttaa ctaattgcgg tttcatagga	839												
tatataaatg tttcaagcca ttattgctga atggttcttt agttattaac ctagacccaa	899												
atcaaagacc agttggattt atgatatttt ttatttgttc ttgcagccaa agtgccagtt	959												
tctttaatat gtgaccaaga acacaaggag catccatatg gccaaataaa tacactgaat	1019												
tttagaaaaa caaaaaaaaa ar	1041												

<210> 374

<211> 1164

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 72..545

<221> sig\_peptide

<222> 72..203

<223> Von Heijne matrix score 5.5 seq ILFFTGWWIMIDA/AV

<221> polyA\_site <222> 1151..1162

<400> 374

aaagtcggcg tggacgtttg aggaagctgg g	atacagcat ttaatgaaaa atttatgctt 60
aagaagtaaa a atg gca ggc ttc cta g	at aat ttt cgt tgg cca gaa tgt 110
Met Ala Gly Phe Leu A	sp Asn Phe Arg Trp Pro Glu Cys
-40	-35
gas tot att dag tod adt dag ada ad	a sat act ata aca tot att atc 158

gaa tgt att gac tgg agt gag aga aga aat gct gtg gca tct gtt gtc Glu Cys Ile Asp Trp Ser Glu Arg Arg Asn Ala Val Ala Ser Val Val

	-30					-25			•		-20					
														gca		206
	Gly	Ile	Leu	Phe		Thr	Gly	Trp	Trp		Met	Ile	Asp	Ala	Ala	
-15					-10					-5					1	254
														aca Thr		254
Val	vaı	IÀT	5	пуs	PIO	ĢIU	GIII	10	ASII	nis	WIG	FIIC	15	1111	Cys	
aat	qta	ttt	tcc	aca	ttq	qct	ttc		atq	ata	aat	gct		tcc	aat	302
														Ser		
_		20	•	•			25					30				
														aga		350
Ala		Val	Arg	Gly	Asp		Tyr	Glu	Ser	Gly		Leu	Gly	Arg	Thr	
	35					40					45			~~~	+	. 398
														Gly 999		390
50	AIG	ALG	vaı	тър	55	FIIC	110	ĢLY	riic	60	БСС	1100	1 110	O Z J	65	
	att	act	tcc	atq		att	ctt	ttt	ggt		tat	gtt	ácc	caa	aat	446
														Gln		
				70					75					80		
act	gat	gtt	tat	ccg	gga	cta	gct	gtg	ttt	ttt	caa	aat	gca	ctt	ata	494
Thr	Asp	Val		Pro	Gly	Leu	Ala		Phe	Phe	Gln	Asn		Leu	Ile	
			85	-+-	a t a	+		90	~~~	200	200	~ .	95 ~~~	cta	taa	542
		_		_						_		-		cta Leu		. 342
FIIC	FIIE	100	1111	пец	116	ıyı	105	FIIC	Gly	Arg	1111	110	OIU	LCu	115	
acc	tga	gatca	act	tctt	aagt	ca c		tcct	t ttg	gtta	tatt	ctg	tttg	tag		595
Thr					_							_				
															atgttt	655
_			,	•	_	-									tatttt	715
															tgagta	775 835
															catcat	895
															tgcctg tgagac	955
															gcatgg	1015
_	_	_			_										gaaccc	1075
															gagaaa	1135
gtg	aaac	tcc (	ctct	caaa	aa a	aaaa	aamc									1164

<210> 375 <211> 1250 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 36..425 <221> sig\_peptide <222> 36..119 <223> Von Heijne matrix score 11.6000003814697 seq LLLLVQLLRFLRA/DG <221> polyA\_signal <222> 1215..1220 <221> polyA\_site <222> 1240..1250

atttcttccc cccgagctgg gcgtgcgcgg ccgca atg aac tgg gag ctg ctg  Met Asn Trp Glu Leu Leu  -25	53
ctg tgg ctg ctg gtg ctg tgc gcg ctg ctc ctg ctc ttg gtg cag ctg Leu Trp Leu Leu Val Leu Cys Ala Leu Leu Leu Leu Leu Val Gln Leu -20 -15 -10	101
ctg cgc ttc ctg agg gct gac ggc gac ctg acg cta cta tgg gcc gag Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu Thr Leu Leu Trp Ala Glu -5 1 5 10	149
tgg cag gga cga cgc cca gaa tgg gag ctg act gat atg gtg gtg tgg Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu Thr Asp Met Val Val Trp 15 20 25	197
gtg act gga gcc tcg agt gga att ggt gag gag ctg gct tac cag ttg Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu Ala Tyr Gln Leu 30 35 40	245
tct aaa cta gga gtt tct ctt gtg ctg tca gcc aga aga gtg cat gag Ser Lys Leu Gly Val Ser Leu Val Leu Ser Ala Arg Arg Val His Glu 45 50 55	293
ctg gaa agg gtg aaa aga aga tgc cta gag aat ggc aat tta aaa gaa Leu Glu Arg Val Lys Arg Arg Cys Leu Glu Asn Gly Asn Leu Lys Glu 60 65 70	341
aaa gat ata ctt gtt ttg ccc ctt gac ctg acc gac act ggt tcc cat Lys Asp Ile Leu Val Leu Pro Leu Asp Leu Thr Asp Thr Gly Ser His 75 80 85 90	389
gaa agc ggc tac caa agc tgt tct cca gga att tgg tagaatcgac Glu Ser Gly Tyr Gln Ser Cys Ser Pro Gly Ile Trp 95 100	435
attctggtca acaatgtgga aatgtcccag cgttctctgt gcatggatac caacttggat	495
gtctacagaa agctaatgag agcttaacta cttagggacg gtgtccttga caaaatgtgk	555. 615
kctgcctcac atgatcgaga ngaarcaagg aaagattgtt actgtgaata gcatcctggg tatcatatct gtacctcttt ccattggata ctgtgctagc aagcatgctc tccggggktk	675
ktttaatggc cttcraacag aacttgccac atacccargt ataatagttt ctaacatttg	735
cccaggacct gtgcaatcaa atattgtgga aaattcccta gctggagaag tcacaaagac	795
tataggcaat aatggagacc agtcccacaa gatgacaacc agtcgttgtg tgcggctgat	855
gttaatcagc atggccaatg atttgaaaga agtttggatc tcagaacaac ctttcttgtt	915
agtaacatat ttgtggcaat acatgccaac ctgggcctgg tggataacca acaagatggg	975
gaagaaaagg attgagaact ttaagagtgg tgtggatgca gactcttctt attttaaaat	1035
ctttaagaca aaacatgact gaaaagagca cctgtacttt tcaagccact ggagggagaa	1095 1155
atggaaaaca tgaaaacagc aatcttctta tgcttctgaa taatcaaaga ctaatttgtg attttacttt ttaatagata tgactttgct tccaacatgg aatgaaataa aaaataaata	1215
ataaaagatt gccatgaatc ttgcaaaaaa aaaaa	1250

```
<210> 376
```

<220>

<221> CDS

<222> 155..751

<221> sig\_peptide

<222> 155..340

<223> Von Heijne matrix
 score 3.70000004768372
 seq SILGIISVPLSIG/YC

<221> polyA\_signal

<222> 912..917

<sup>&</sup>lt;211> 947

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Homo sapiens

<221> polyA\_site <222> 937..947

	<400	> 37	6														
				gatg	ccta	g ag	gaatg	gcaa	ttt	aaaa	gaa	aaaç	atat	ac t	tgtt	ttgcc	60
	cctt	gaco	tg a	iccga	cact	g gt	tccc	atga	ago	ggct	acc	aaag	ctgt	tc t	ccag	gagtt	120
	tggt	agaa	itc s	gacat	tctg	g to	caaca	atgg	tgg	ja at	g to	c ca	ig cg	gt to	t ct	g tgc	175
	Met Ser Gln Arg Ser Leu Cys																
-60 atg gat acc agc ttg gat gtc tac aga rag cta ata gag ctt aac tac																	
	atg	gat	acc	agc	ttg	gat	gtc	tac	aga	rag	cta	ata	gag	ctt	aac	tac	223
	Met	Āsp	Thr	Ser	Leu	Asp	Val	Tyr	Arg	Xaa	Leu	Ile	Glu	Leu	Asn	Tyr	
•	-55					-50					-45					-40	
	tta	ggg	acg	gtg	tcc	ttg	aca	aaa	tgt	gtt	ctg	cct	cac	atg	atc	gag	271
	Leu	Gly	Thr	Val	Ser	Leu	Thr	Lys	Cys	Val	Leu	Pro	His	Met	Ile	Glu	
					-35					-30					-25		
	agg	aag	caa	gga	aag	att	gtt	act	gtg	aat	agc	atc	ctg	ggt	atc	ata	319
	Arg	Lys	Gln	Gly	Lys	Ile	Val	Thr	Val	Asn	Ser	Ile	Leu	Gly	Ile	Ile	
				-20					-15					-10			
	tct	gta	cct	ctt	tcc	att	gga	tac	tgt	gct	agc	aag	cat	gct	ctc	cgg	.367
	Ser	Val	Pro	Leu	Ser	Ile	Gly	Tyr	Cys	Ala	Ser	Lys	His	Ala	Leu	Arg	
			-5					1				5					
	ggt	ttt	ttt	aat	ggc	ctt	cga	aca	gaa	ctt	gcc	aca	tac	cca	ggt	ata	415
	Gly	Phe	Phe	Asn	Gly	Leu	Arg	Thr	Glu	Leu		Thr	Tyr	Pro	Gly	Ile	
	10					15					20					25	
	ata	gtt	tct	aac	att	tgc	cca	gga	cct	gtg	caa	tca	aat	att	gtg	gaa	463
	Ile	Val	Ser	Asn	Ile	Cys	Pro	Gly	Pro		Gln	Ser	Asn	Ile	Val	Glu	
					30					35					40		<b></b>
	aat	tcc	cta	gct	gga	gaa	gtc	aca	aaa	act	ata	ggc	aat	aat	gga	aac	511
	Asn	Ser	Leu	Ala	Gly	Glu	Val	Thr		Thr	Ile	Gly	Asn		Gly	Asn	•
				45					50					55			550
	cag	tcc	cac	aag	atg	aca	acc	agt	cgt	tgt	gtg	cgg	ctg	atg	tta	atc	559
	Gln	Ser		Lys	Met	Thr	Thr		Arg	Cys	Val	Arg		Met	Leu	11e	
			60					65					70			++-	607
	agc	atg	gcc	aat	gat	ttg	aaa	gaa	gtt	tgg	atc	tca	gaa	Caa	cct	Dho	807
	Ser		Ala	Asn	Asp	Leu		GIu	vaı	Trp	11e		GIU	GIN	Pro	Phe	
		75					80					85	<b>.</b>	~~~	+~~	taa	655
	ttg	tta	gta	aca	tat	ttg	tgg	caa	tac	atg	CCa	acc	~~~	712	tgg	Trn	055
		Leu	Val	Thr	Tyr		Trp	GIN	Tyr	met		Thr	пр	A.la	Trp	105	
	90	•				95					100			224	act		703
	ata	acc	aac	aag	atg	999	aag	aaa	agg	TIO	gag	aac Nan	Dho	Larg	agt	Glv	, 05
	TIE	Thr	Asn	гÀг		GIY	ьys	ьys	Arg		GIU	ASII	FIIC	пуз	Ser 120	Gry	
					110					115			202	222		asc.	751
	gtg	gat	gem	rac	tct	CCU	Tat	Dho	aaa	TIO	Dho	aay	Thr	Tare	cat	Aen	, , , ,
	vaı	Asp	Ala		ser	Ser	Tyr	PHE	130	TIE	Pne	nys	1111	135	His	wob	
				125	~+	++ +	+ < = =	~~~		aaaa	asas	aa+	aaaa			aaacag	811
	tga	aaag tott	anc	acct	yıac ++~+	ul [	tast	guud	a sa	9299 +==+	9aya ++a+	aat	99aa +++2	ctt	ttta	atagat	871
	caa			arge		ya a +	raal	-aad	9 ac	222+	222+	gat aat	2222	gat	tacc	atgrrt	931
						ra a	TILG	aaat	u aa	uaal	uaat	aat	uuaa	gut	-5-0		947
	CLC	ycaa	aad	aaaa	aa												

<210> 377

<211> 621

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 46..585

<221> sig\_peptide

<222> 46..120 u, <223> Von Heijne matrix score 6.30000019073486 seq AFSLSVMAALTFG/CF <221> polyA signal <222> 584..589 <221> polyA\_site \_ <222> 606..619... <400> 377 aactgggtgt gcgtrtggag tccggactcg tgggagacga tcgcg atg aac acg gtg Met Asn Thr Val ctg tcg cgg gcg aac tca ctg ttc gcc ttc tcg ctg agc gtg atg gcs 105 Leu Ser Arg Ala Asn Ser Leu Phe Ala Phe Ser Leu Ser Val Met Ala -15 -10 gcg ctc acc ttc ggc tgc ttc atc ayy acc gcc ttc aaa gac agg agc 153 Ala Leu Thr Phe Gly Cys Phe Ile Xaa Thr Ala Phe Lys Asp Arg Ser ..1 -5 gtc ccg gtg cgg ctg cac gtc tcg cga atc atg cta aaa aat gta gaa 201 Val Pro Val Arg Leu His Val Ser Arg Ile Met Leu Lys Asn Val Glu 15 20 gat ttc act gga cct aga gaa aga agt gat ctg gga ttt atc aca ttt 249 Asp Phe Thr Gly Pro Arg Glu Arg Ser Asp Leu Gly Phe Ile Thr Phe 35 gat ata act gct gat cta gag aat ata ttt gat tgg aat gtt aag cag 297 Asp Ile Thr AlamAsp Leu Glu Asn Ile Phe Asp Trp Asn' Val Lys Gln 50 ttg ttt ctt tat..tta tca gca gaa tat tca aca aaa aat aat gct ctg 345 Leu Phe Leu Tyr Leu Ser Ala Glu Tyr Ser Thr Lys Asn Asn Ala Leu 65 70 aac caa ktt gtc cta tgg gac aag att gtt ttg aga ggt gat aat ccg 393 Asn Gln Xaa Val Leu Trp Asp Lys Ile Val Leu Arg Gly Asp Asn Pro 85 aag ctg ctg ctg aaa gat atg aaa aca aaa tat ttt ttc ttt gac gat 441 Lys Leu Leu Lys Asp Met Lys Thr Lys Tyr Phe Phe Asp Asp 100 gga aat ggt ctc wag gga aac agg aat gtc act ttg acc ctg tct tgg 489 Gly Asn Gly Leu Xaa Gly Asn Arg Asn Val Thr Leu Thr Leu Ser Trp 115 aac gtc gta cca aat gct gga att cta cct ctt gtg aca gga tca gga 537 Asn Val Val Pro Asn Ala Gly Ile Leu Pro Leu Val Thr Gly Ser Gly 130 cac gta tct gtc cca ttt cca gat aca tat gaa ata acg aag agt tat 585 His Val Ser Val Pro Phe Pro Asp Thr Tyr Glu Ile Thr Lys Ser Tyr 150 taaattatto tgaatttgaa acaaaaaaa aaaahm 621

<210> 378

<211> 52

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -20..-1

<400> 378

Met Pro Ser Val Asn Ser Ala Gly Leu Cys Val Leu Gln Leu Thr Thr -10 -15 -20 Ala Val Thr Ser Ala Phe Leu Leu Ala Lys Val Asn Pro Phe Glu Xaa 1 Phe Leu Ser Arg Gly Phe Trp Leu Cys Ala Ala His His Phe Ile His 20 Pro Cys Leu Asp 30

<210> 379 <211> 193 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -23..-1

<400> 379

Met Val Val Leu Arg Ala Gly Lys Lys Thr Phe Leu Pro Pro Leu Xaa -20 -15 Arg Ala Phe Ala Cys Arg Gly Cys Gln Leu Ala Pro Glu Arg Gly Ala 1 Glu Arg Arg Asp Thr Ala Pro Ser Gly Val Ser Arg Phe Cys Pro Pro 20 10 Arg Lys Ser Cys His Asp Trp Ile Gly Pro Pro Asp Lys Tyr Ser Asn 30 Leu Arg Pro Val His Phe Tyr Ile Pro Glu Asn Glu Ser Pro Leu Glu 50 45 Gln Lys Leu Arg Lys Leu Arg Gln Glu Thr Gln Glu Trp Asn Gln Gln 65 Phe Trp Ala Asn Gln Asn Leu Thr Phe Ser Lys Glu Lys Glu Glu Phe Ile His Ser Arg Leu Lys Thr Lys Gly Leu Gly Leu Arg Thr Glu Ser 100 95 Gly Gln Lys Ala Thr Leu Asn Ala Glu Glu Met Ala Asp Phe Tyr Lys 115 ·· 110 Glu Phe Leu Ser Lys Asn Phe Gln Lys His Met Tyr Tyr Asn Arg Asp 130 Trp Tyr Lys Arg Asn Phe Ala Ile Thr Phe Phe Met Gly Lys Val Ala 140 145 Leu Glu Arg Ile Trp Asn Lys Leu Lys Gln Lys Gln Lys Lys Arg Ser 160

<210> 380 <211> 82 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -14..-1

Asn 170

> <400> 380 Met Ala Phe Thr Leu Xaa Ser Leu Leu Gln Ala Ala Leu Leu Cys Val

WO 99/31236 -294 - PCT/IB98/02122

```
Asn Ala Ile Ala Val Leu His Glu Glu Arg Phe Leu Lys Asn Ile Gly
                            10
Trp Gly Thr Asp Gln Gly Ile Gly Gly Phe Gly Glu Glu Pro Gly Ile
                        25
Lys Ser Xaa Xaa Met Xaa Leu Ile Arg Ser Val Arg Thr Val Met Arg
                    40
                                        45
Val Pro Leu Ile Ile Val Asn Ser Ile Ala Ile Val Leu Leu Leu Leu
Phe Gly
<210> 381
<211> 198
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 381
Met Pro Val Pro Ala Leu Cys Leu Leu Trp Ala Leu Ala Met Val Thr
                        -15
Arg Pro Ala Ser Ala Ala Pro Met Gly Gly Pro Glu Leu Ala Gln His
Glu Glu Leu Thr Leu Leu Phe His Gly Thr Leu Gln Leu Gly Gln Ala
Leu Asn Gly Val Tyr Arg Thr Thr Glu Gly Arg Leu Thr Lys Ala Arg
Asn Ser Leu Gly Leu Tyr Gly Arg Thr Ile Glu Leu Leu Gly Gln Glu
Val Ser Arg Gly Arg Asp Ala Ala Gln Glu Leu Arg Ala Ser Leu Leu
                    65
                                         70
Glu Thr Gln Met Glu Glu Asp Ile Leu Xaa Leu Gln Ala Xaa Ala Thr
                                     85
Ala Glu Val Leu Gly Glu Val Ala Gln Ala Gln Lys Val Leu Arg Asp
                                 100
Ser Val Gln Arg Leu Xaa Xaa Gln Leu Xaa Xaa Ala Trp Leu Gly Pro
                             115
                                                 120
Ala Tyr Arg Lys Phe Glu Val Leu Lys Ala Pro Pro Xaa Lys Gln Asn
                         130
                                             135
His Ile Leu Trp Ala Leu Thr Gly His Val Xaa Arg Gln Xaa Arg Glu
                                         150
Met Val Ala Gln Gln Xaa Xaa Leu Xaa Gln Ile Gln Glu Lys Leu His
                160
                                     165
Thr Ala Ala Leu Pro Ala
            175
<210> 382
<211> 160
 <212> PRT
 <213> Homo sapiens
<220>
 <221> SIGNAL
 <222> -55..-1
```

Met Asp Lys Leu Lys Lys Val Leu Ser Gly Gln Asp Thr Glu Asp Arg

-45 -50 -55 Ser Gly Leu Ser Glu Val Val Glu Ala Ser Ser Leu Ser Trp Ser Thr -30 -35 Arg Ile Lys Gly Phe Ile Ala Cys Phe Ala Ile Gly Ile Leu Cys Ser -15 -20 Leu Leu Gly Thr Val Leu Leu Trp Val Pro Arg Lys Gly Leu His Leu Phe Ala Val Phe Tyr Thr Phe Gly Asn Ile Ala Ser Ile Gly Ser Thr 15 Ile Phe Leu Met Gly Pro Val Lys Gln Leu Lys Arg Met Phe Glu Pro ...35 30 Thr Arg Leu Ile Ala Thr Ile Met Val Leu Leu Cys Phe Ala Leu Thr 50 45 Leu Cys Ser Ala Phe Trp Trp His Asn Lys Gly Leu Ala Leu Ile Phe 70 65 Cys Ile Leu Gln Ser Leu Ala Leu Thr Trp Tyr Ser Leu Ser Phe Ile 80 Pro Phe Ala Arg Asp Ala Val Lys Xaa Cys Phe Ala Val Cys Leu Ala 100

<210> 383 <211> 108 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -18..-1

<210> 384 <211> 64 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -22..-1

```
1
Leu Tyr Ile Pro Xaa Arg Xaa Arg Ser Asp Glu Leu Val Phe Glu Ser
                    20
           15
Gln Lys Gly Ser Ala Met Glu Leu Ala Val Ile Thr Val Xaa Gly Val
                      35
<210> 385 " "
<211> 27
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 385
Met Gly Phe Leu Xaa Leu Met Thr Leu Thr Thr His Val His Ser Ser
-15 -10 -5
Ala Lys Pro Asn Glu Gln Pro Trp Leu Leu Asn
<210> 386
<211> 186
<212> PRT
<213> Homo sapien's
<220>
<221> SIGNAL
<222> -21..-1
Met Ser Pro Ser Gly Arg Leu Cys Leu Leu Thr Ile Val Gly Leu Ile
                     -15
                             -10
Leu Pro Thr Arg Gly Gln Thr Leu Lys Asp Thr Thr Ser Ser Ser
Ala Asp Ser Thr Ile Met Asp Ile Gln Val Pro Thr Arg Ala Pro Asp
                             20
Ala Val Tyr Thr Glu Leu Gln Pro Thr Ser Pro Thr Pro Thr Trp Pro
                         35
Ala Asp Glu Thr Pro Gln Pro Gln Thr Gln Thr Gln Gln Leu Glu Gly
                     50
Thr Asp Gly Pro Leu Val Thr Asp Pro Glu Thr His Xaa Ser Xaa Lys
                                    70
Ala Ala His Pro Thr Asp Asp Thr Thr Thr Leu Ser Glu Arg Pro Ser
                                 85
Pro Ser Thr Xaa Val His Xaa Arg Pro Xaa Xaa Pro Ser Xaa His Leu
                             100
Val Phe Met Arg Met Thr Pro Ser Ser Met Met Asn Thr Pro Ser Gly
                         115
                                           120
Asn Xaa Gly Cys Trp Ser Gln Leu Cys Cys Ser Ser Gln Ala Ser Ser
                     130
                                        135
Ser Ser Pro Val Ala Ser Ala Gly Ser Cys Pro Gly Tyr Ala Gly Ile
                 145
```

Ile Ala Gly Glu Ser Ile Arg Asn Arg Ser 160 165 11

```
<210> 387
<211> 179
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1
<400> 387
Met Glu Thr Gly Ala Leu Arg Arg Pro Gln Leu Leu Pro Leu Leu
                                            -15
                        -20
Leu Leu Cys Gly Pro Ser Gln Asp Gln Cys Arg Pro Val Leu Gln Asn
Leu Leu Gln Ser Pro Gly Leu Thr Trp Ser Leu Glu Val Pro Thr Gly
Arg Glu Gly Lys Glu Gly Gly Asp Arg Gly Pro Gly Leu Xaa Gly Ala
                            30
Thr Pro Ala Arg Ser Pro Gln Gly Lys Glu Met Gly Arg Gln Arg Thr
                        45
Arg Lys Val Lys Gly Pro Ala Trp Xaa His Thr Ala Asn Gln Glu Leu
Asn Arg Met Arg Ser Leu Ser Ser Gly Ser Val Pro Val Gly His Leu
                                    80
Glu Gly Gly Thr Val Lys Leu Gln Lys Asp Thr Gly Leu His Ser Cys
Xaa Asp Gly Met Ala Ser Leu Glu Gly Thr Pro Ala Ser Val Leu Ala
                            110
       105
Asp Ala Cys Pro Gly Phe His Asp Val Xaa Val Gln Xaa Ala Leu Phe
                       125
                                            130
Gly Leu Ser Gly Xaa Xaa Leu Trp Leu Lys Thr His Phe Cys Leu Ser
                                        145
                   140
Ile Xaa Leu
 <210> 388
 <211> 150
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -55..-1
 Met Ala Thr Thr Val Pro Asp Gly Cys Arg Asn Gly Leu Lys Ser Lys
                     -50
 Tyr Tyr Arg Leu Cys Asp Lys Ala Glu Ala Trp Gly Ile Val Leu Glu
                                     -30
 Thr Val Ala Thr Ala Gly Val Val Thr Ser Val Ala Phe Met Leu Thr
                                  -15
             -20
 Leu Pro Ile Leu Val Cys Lys Val Gln Asp Ser Asn Arg Arg Lys Met
 Leu Pro Thr Gln Phe Leu Phe Leu Leu Gly Val Leu Gly Ile Phe Gly
                                         20
 Leu Thr Phe Ala Phe Ile Ile Gly Leu Asp Gly Ser Thr Gly Pro Thr
                 30
 Arg Phe Phe Leu Phe Gly Ile Leu Phe Ser Ile Cys Phe Ser Cys Leu
                                  50
```

Leu Aļa His Ala Val Ser Leu Thr Lys Leu Val Arg Gly Arg Lys Ala

```
Pro Phe Pro Val. Gly Asp Ser Gly Ser Gly Arg Gly Leu Gln Pro Ser
   75
                      80
                                          85
Pro Gly Cys Tyr Arg Tyr
<210> 389
<211> 236
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -31..-1
<400> 389
Met Leu Ser Lys Gly Leu Lys Arg Lys Arg Glu Glu Glu Glu Glu Lys
                       -25
                                           -20
Glu Pro Leu Ala Val Asp Ser Trp Trp Leu Asp Pro Gly His Ala Ala
                  -10
                                   · -5
Val Ala Gln Ala Pro Pro Ala Val Ala Ser Ser Ser Leu Phe Asp Leu
                       . . 10
Ser Val Leu Lys Leu His His Ser Leu Gln Xaa Ser Xaa Pro Asp Leu
                          25
Arg His Leu Val Leu Val Xaa Asn Thr Leu Arg Arg Ile Gln Ala Ser
                       40
Met Ala Pro Ala Ala Ala Leu Pro Pro Val Pro Thr Pro Pro Ala Ala
        1 55
                                      60
Pro Xaa Val Ala Asp Asn Leu Leu Ala Ser Ser Asp Ala Ala Leu Ser
              .70
                                   75
Ala Ser Met Ala Xaa Leu Leu Glu Asp Leu Ser His Ile Glu Gly Leu
                               90
Ser Gln Ala Pro Gln Pro Leu Ala Asp Glu Gly Pro Pro Gly Arg Ser
                          105
                                              110
Ile Gly Gly Xaa Pro Pro Xaa Leu Gly Ala Leu Asp Leu Leu Gly Pro
                       120
                                           125
Ala Thr Gly Cys Leu Leu Asp Asn Gly Leu Glu Gly Leu Phe Glu Asp
                                       140
                   135
Ile Asp Thr Ser Met Tyr Asp Asn Glu Leu Trp Ala Pro Ala Ser Glu
                                   155 ' 160
                150
Gly Leu Lys Pro Gly Pro Glu Asp Gly Pro Gly Lys Glu Glu Ala Pro
                               170
Glu Leu Asp Glu Ala Glu Leu Asp Tyr Leu Met Asp Val Leu Val Gly
                           185
Thr Gln Ala Leu Glu Arg Pro Pro Gly Pro Gly Arg
                       200
 <210> 390
 <211> 149
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -100..-1
 <400> 390
```

Met Glu Thr Leu Tyr Arg Val Pro Phe Leu Val Leu Glu Cys Pro Asn

WO 99/31236 -299- PCT/IB98/02122

```
Leu Lys Leu Lys Lys Pro Pro Trp Leu His Met Pro Ser Ala Met Thr
                -80
                                   -75
Val Tyr Ala Leu Val Val Val Ser Tyr Phe Leu Ile Thr Gly Gly Ile
                                                  -55
                            -60
Ile Tyr Asp Val Ile Val Glu Pro Pro Ser Val Gly Ser Met Thr Asp
                                              -40
        -50
               . -45
Glu His Gly His Gln Arg Pro Val Ala Phe Leu Ala Tyr Arg Val Asn
                                          -25
                       -30
Gly Gln Tyr Ile Met Glu Gly Leu Ala Ser Ser Phe Leu Phe Thr Met
         -15
                                    -10
Gly Gly Leu Gly Phe Ile Ile Leu Asp Gly Ser Asn Ala Pro Asn Ile
                                                   10
                1 .
                               5.
Pro Lys Leu Asn Arg Phe Leu Leu Leu Phe Ile Gly Phe Val Cys Val
                           20
Leu Xaa Ser Phe Xaa Xaa Ala Arg Val Phe Met Arg Met Lys Leu Pro
Gly Tyr Leu Met Gly
<210> 391
<211> 69
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -49..-1
<400> 391
Met Pro Phe His Phe Pro Phe Leu Gly Phe Val Cys Leu His Leu His
                -45
                                   -40
Leu Thr Pro Cys Leu Thr Val Pro Arg Arg Pro Leu Phe Leu Leu
                                                   -20
            -30
                                -25
His Leu Cys Pro His Leu Pro Phe Leu Leu Leu Ser Cys Val Gly
        -15
                            -10
 Xaa Xaa Pro Ser Cys Leu Pro Ser Ser Ser Thr Cys Val Ser Leu His
 Phe Phe Ile Pro Asp
                20
 <210> 392
 <211> 241
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -30..-1
 <400> 392
 Met Gly Thr Ala Ser Arg Ser Asn Ile Ala Arg His Leu Gln Thr Asn
                                        -20
                     -25
 Leu Ile Leu Phe Cys Val Gly Ala Val Gly Ala Cys Thr Leu Ser Val
                                     - 5
                 -10
 Thr Gln Pro Trp Tyr Leu Glu Val Asp Tyr Thr His Glu Ala Val Thr
                                                15
                             10
```

Ile Lys Cys Thr Phe Ser Ala Thr Gly Cys Pro Ser Glu Gln Pro Thr

Cys Leu Trp PHe Arg Tyr Gly Ala His Gln Pro Glu Asn Leu Cys Leu 40 Asp Gly Cys Lys Ser Glu Ala Xaa Lys Phe Thr Val Arg Glu Ala Leu 60 Lys Glu Asn Gln Val Ser Leu Thr Val Asn Arg Val Thr Ser Asn Asp 70 75 Ser Ala Ile Tyr Ile Cys Gly Ile Ala Phe Pro Ser Val Pro Glu Ala Arg Ala Lys Gln Thr Gly Gly Gly Thr Thr Leu Val Val Arg Glu Ile 105 110 Lys Leu Leu Ser Lys Glu Leu Arg Ser Phe Leu Thr Ala Leu Val Ser 125 115 120 Leu Leu Ser Val Tyr Val Thr Gly Val Cys Val Ala Phe Ile Leu Leu 140 135 Ser Lys Ser Lys Ser Asn Pro Leu Arg Asn Lys Glu Ile Lys Glu Asp 150 155 Ser Gln Lys Lys Ser Ala Arg Arg Ile Phe Gln Glu Ile Ala Gln 170 175 Glu Leu Tyr His Lys Arg His Val Glu Thr Asn Gln Gln Ser Glu Lys 190 e 185 Asp Asn Asn Thr Tyr Glu Asn Arg Arg Val Leu Ser Asn Tyr Glu Arg 200 205 Pro

<210> 393
<211> 47
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL

<400> 393

<222> -30..-1

 Met Asn Cys Asn Val Val Ser Glu Arg Gly Lys Trp Leu Glu Val Glu

 -30
 -25
 -20
 -15

 Cys Ser Leu Met Thr Cys Thr Thr Leu Ile Asn Ala Ser Ala Ile Ser
 -10
 -5
 1

 Thr Asn Thr Leu Thr Asp Met Gly Ser Phe Asp Arg Arg Glu Ser
 5
 15

<210> 394 <211> 65 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -28..-1

<400> 394

 Met Ala
 Phe Gly Leu Gln Met Phe Ile Gln Arg Lys Phe Pro Tyr Pro -25
 -20
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 -15
 <t

35 25 30

Ser

<210> 395

<211> 73

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -24..-1

·<400> 395

Met Thr Cys Trp Met Leu Pro Pro Ile Ser Phe Leu Ser Tyr Leu Pro -20

-15

Leu Trp Leu Gly Pro Ile Trp Pro Cys Ser Gly Ser Thr Leu Gly Lys -5 1

Pro Asp Pro Gly Val Trp Pro Ser Leu Phe Arg Pro Trp Asp Ala Ala 15 20

Ser Pro Gly Asn Tyr Ala Leu Ser Arg Gly Xaa Asn Xaa Tyr Xaa Xaa

30 35

Trp Gly Gln Gly Thr His Ser Ser Leu

<210> 396

<211> 60

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -18..-1

<400> 396

Met Pro Cys Pro Thr Trp Thr Cys Leu Lys Ser Phe Pro Ser Pro Thr -15

-10

Ser Ser His Ala Ser Ser Leu His Leu Pro Pro Ser Cys Thr Arg Leu 10

Thr Leu Thr Gln Thr Leu Arg Thr Gly Met His Leu Ser Arg Ala Leu

20 25

Gln Gly Thr Leu Thr Arg Leu Gln Ser Thr Pro Ala 35

<210> 397

<211> 192

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -93..-1

<400> 397

Met Ala Glu Leu Gly Leu Asn Glu His His Gln Asn Glu Val Ile Asn

-90 -85

Tyr Met Arg Phe Ala Arg Ser Lys Arg Gly Leu Arg Leu Lys Thr Val

-75 -70 Asp Ser Cys Phe Gln Asp Leu Lys Glu Ser Arg Leu Val Glu Asp Thr -55 -50 Phe Thr Ile Asp Glu Val Ser Glu Val Leu Asn Gly Leu Gln Ala Val -40 -35 Val His Ser Glu Val Glu Ser Glu Leu Ile Asn Thr Ala Tyr Thr Asn -25 -20 Val Leu Leu Arg Gln Leu Phe Ala Gln Ala Glu Lys Trp Tyr Leu -10 - 5 Lys Leu Gln Thr Asp Ile Ser Glu Leu Glu Asn Arg Glu Leu Leu Glu 10 Gln Xaa Ala Glu Phe Glu Lys Ala Xaa Ile Thr Ser Ser Asn Lys Lys 25 Pro Ile Leu Xaa Val Thr Xaa Pro Lys Leu Ala Pro Leu Asn Glu Gly Gly Thr Ala Lys Leu Leu Asn Lys Val Ile Cys Ile Ile Leu Arg Asn 60 Gly Lys Ser Leu Ile Leu Ser Cys His Cys Leu Gly Trp Arg Asn Lys Ser Gly Arg Phe Val Ser Gly Pro Leu Arg Ile Ile Ser Pro Leu Gln

<210> 398 <211> 149 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -72..-1

<400> 398

Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr Ile Ser Ile Phe -65 Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro Ile Gln Ala Leu -50 Met Ala Ile Ser Ala Thr Phe Lys Met Leu Glu Ser Ser Ser Gln Lys -30 Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu Met Gly Leu Ala -20 -15 Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu Pro Thr His Ala Ser Asp Trp Leu Ala Phe Ile Glu Pro Pro Glu Arg Met Glu Ser Val 15 Val Glu Asp Cys Phe Cys Glu His Glu Lys Ala Ala Pro Gly Pro Tyr 30 35 Val Phe Gly Ser Tyr Leu His Pro Ser Leu Ser Pro Val Ala Pro Gln His Thr Leu Lys Leu Ile Thr Tyr Val Lys Lys Asn Gln Lys Thr Leu Phe Ser Met Val Gly

<210> 399 <211> 73 <212> PRT <213> Homo sapiens

```
WO 99/31236
```

<220> <221> SIGNAL <222> -20..-1

<400> 399

Met Thr Pro Leu Leu Thr Leu Ile Leu Val Val Leu Met Gly Leu Pro -10 -15

Leu Ala Gln Ala Leu Asp Cys His Val Cys Ala Tyr Asn Gly Asp Asn 1

Cys Phe Asn Pro Met Arg Cys Pro Ala Met Val Ala Tyr Cys Met Thr 20

Thr Arg Thr Tyr Tyr Thr Pro Thr Arg Met Lys Val Ser Lys Ser Cys 35

Val Pro Arg Cys Phe Glu Xaa Cys Val

<210> 400 <211> 86

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -20..-1

<400> 400

Met Asn Leu His Phe Pro Gln Trp Phe Val His Ser Ser Ala Leu Gly -5 -10 -15

Leu Val Leu Ala Pro Pro Phe Ser Ser Pro Gly Thr Asp Pro Thr Phe 1

Pro Cys Ile Tyr Cys Arg Leu Leu Asn Met Ile Met Thr Arg Leu Ala 20

Phe Ser Phe Ile Thr Cys Leu Cys Pro Asn Leu Lys Glu Val Cys Leu 35

Ile Leu Pro Glu Lys Asn Cys Asn Ser Arg His Ala Gly Phe Val Gly 55

Pro Xaa Lys Leu Arg Gln

65

<210> 401

<211> 78

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -21..-1

<400> 401

Met Cys Pro Val Phe Ser Lys Gln Leu Leu Ala Cys Gly Ser Leu Leu -10 -15

Pro Gly Leu Trp Gln His Leu Thr Ala Asn His Trp Pro Pro Phe Ser

Xaa Phe Leu Cys Thr Val Cys Ser Gly Ser Ser Glu Gln Ile Ser Glu 20

Tyr Thr Ala Ser Ala Thr Pro Pro Leu Cys Arg Ser Leu Asn Gln Glu 35

Pro Phe Val Ser Arg Ala Ile Arg Pro Lys Tyr Ser Ile Thr

45

50

55

```
<210> 402
<211> 65
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -28..-1
<400> 402
Met Gly Lys Gly His Gln Arg Pro Trp Trp Lys Val Leu Pro Leu Ser
           -25
                                -20
                                                    -15
Cys Phe Leu Val Ala Leu Ile Ile Trp Cys Tyr Leu Arg Glu Glu Ser
Glu Ala Asp Gln Trp Leu Arg Gln Val Trp Gly Glu Val Pro Glu Pro
                                 . '15
                  1'0
Ser Asp Arg Ser Glu Glu Pro Glu Thr Pro Ala Ala Tyr Arg Ala Arg
                25
                                    30
Thr
<210> 403
<211> 211
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27..-1
<400> 403
Met Leu Leu Leu Ser Ile Thr Thr Ala Tyr Thr Gly Leu Glu Leu Thr
                            -20
Phe Phe Ser Gly Val Tyr Gly Thr Cys Ile Gly Ala Thr Asn Lys Phe
Gly Ala Glu Glu Xaa Ser Leu Ile Gly Leu Ser Gly Ile Phe Ile Gly
Ile Gly Glu Ile Leu Gly Gly Ser Leu Phe Gly Leu Leu Ser Lys Asn
                                30
Asn Arg Phe Gly Arg Asn Pro Val Val Leu Leu Gly Ile Leu Val His
                            45
Phe Ile Ala Phe Tyr Leu Ile Phe Leu Asn Met Pro Gly Asp Ala Pro
Ile Ala Pro Val Lys Gly Thr Asp Ser Ser Ala Tyr Ile Lys Ser Ser
                    75
Lys Xaa Phe Ala Ile Leu Cys Xaa Phe Leu Xaa Gly Leu Gly Asn Ser
                                    95
                90
Cys Phe Asn Thr Xaa Leu Leu Xaa Ile Xaa Gly Phe Leu Tyr Ser Glu
                                110
                                                     115
Xaa Ser Ala Pro Xaa Phe Ala Ile Phe Asn Phe Val Gln Ser Ile Cys
```

125

140

155

170

Ala Ala Val Ala Phe Phe Tyr Ser Asn Tyr Leu Leu Leu His Trp Gln

Leu Leu Val Met Val Ile Phe Gly Phe Xaa Gly Thr Ile Ser Phe Phe

Thr Val Glu Trp Glu Xaa Ala Ala Phe Val Xaa Arg Gly Ser Asp Tyr

130

160

Arg Ser Ile

<210> 405

<210> 404 <211> 123 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -80. -1

<400> 404 Met Ser Thr Trp Tyr Leu Ala Leu Asn Lys Ser Tyr Lys Asn Lys Asp -75 -70 Ser Val Arg lle Tyr Leu Ser Leu Cys Thr Val Ser Ile Lys Phe Thr -55 -60 Tyr Phe His Asp Ile Gln Thr Asn Cys Leu Thr Thr Trp Lys His Ser -35 -45 -40 Arg Cys Arg Phe Tyr Trp Ala Phe Gly Gly Ser Ile Leu Gln His Ser -20 -25 -30 Val Asp Pro Leu Val Leu Phe Leu Ser Leu Ala Leu Leu Val Thr Pro -5 -10 Thr Ser Thr Pro Ser Ala Lys Ile Gln Ser Leu Gln Ile Asp Leu Pro 10 5 Gly Gly Trp Arg Leu Ala Thr Asp Arg Ile Phe Thr Leu Ser Pro Val 20 25 Pro Met Asp Xaa Pro Leu Ile Leu His Gln Leu 40 35

<211> 86 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -26..-1 <400> 405 Met Glu Lys Ser Trp Met Leu Trp Asn Phe Val Glu Arg Trp Leu Ile -15 -20 Ala Leu Ala Ser Trp Ser Trp Ala Leu Cys Arg Ile Ser Leu Leu Pro -5 1 Leu Ile Val Thr Phe His Leu Tyr Gly Gly Ile Ile Leu Leu Leu 10 Ile Phe Ile Ser Ile Xaa Gly Ile Leu Tyr Lys Phe Xaa Asp Val Leu 30

Leu Tyr Phe Pro Xaa Gln Xaa Ser Ser Ser Arg Leu Tyr Asp Ser His

50 '

Ala His Trp Xaa Ser Xaa 55 60

<210> 406 <211> 162 <212> PRT <213> Homo sapiens

```
<220>
<221> SIGNAL
<222> -31..-1
<400> 406
Met Ala Ala Arp Pro Ser Gly Pro Xaa Ala Pro Glu Ala Val Thr
                                   -20
                        -25
Ala Arg Leu Val Gly Val Leu Trp Phe Val Ser Val Thr Thr Gly Pro
                   -10
                                       -5.
Trp Gly Ala Val Ala Thr Ser Ala Gly Gly Glu Glu Ser Leu Lys Cys
                               10
.Glu Asp Leu Lys Val Gly Gln Tyr Ile Cys Lys Asp Pro Lys Ile Asn
                           25
Asp Ala Thr Gln Glu Pro Val Asn Cys Thr Asn Tyr Thr Ala His Val
                        40.
Ser Cys Phe Pro Ala Pro Asn Ile Thr Cys Lys Asp Ser Ser Gly Asn
Glu Thr His Phe Thr Gly Asn Glu Val Gly Phe Phe Lys Pro Ile Ser
             . 70
                                  75
Cys Arg Asn Val Asn Gly Tyr Ser Tyr Asn Glu Gln Ser His Val Ser
                               90
Phe Ser Trp Met Val Gly Ser Arg Ser Ile Leu Pro Trp Ile Pro Cys
       100
                           105
Phe Gly Phe Val Lys Xaa Xaa His Cys Arg Val Xaa Trp Asn Trp Glu
  115
                                         . 125
Pro Asn
130
```

```
<210> 407
<211> 98
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -37..-1
```

<210> 408 <211> 70 <212> PRT <213> Homo sapiens

```
<220>
<221> SIGNAL
<222> -15..-1
<400> 408
Met Arq Phe Leu Pro Cys Cys Leu Leu Trp Ser Val Phe Asn Pro Glu
-15 -10 -5
Ser Leu Asn Cys His Tyr Phe Xaa Xaa Glu Xaa Cys Ile Phe Xaa Ser
Leu Gln Tyr Tyr Glu Ile Ser Leu Gln Glu Lys Leu Leu Gly Phe Leu
                  25 ·
     . 20
Trp Leu Cys Phe Leu Ser Tyr Phe Phe Arg Ala Val Tyr Phe Leu Ile
               40
Asp Phe Ser Ser Phe Thr
<210> 409
<211> 60
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -45..-1
<400> 409
         . . .
Met His Ser Leu Phe Ile Ala Ser Leu Lys Val Leu Phe Tyr Tyr Ser
-45 . -40 -35
Phe Ser Phe Arg Phe Asn Trp Phe Asp Cys Leu Leu His Asn Leu Gly
                               -20
             -25
Glu Asn Phe Leu Ser Leu Leu Ser Lys Ser Cys Ser Ala Asp Pro Ser
                             -5
       -10
Gly Ser Thr Phe Met Arg Asp Ile Glu Thr Asn Lys
                      10
<210> 410
<211> 39
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1
<400> 410
Met Pro Glu Ala Val Glu Gln Ser Ala His Leu Phe Val Thr Trp Ser
                   -15
Ser Gln Arg Ala Leu Ser His Pro Ala Pro Phe Leu Thr Xaa Xaa Lys
                     1
Asn Pro Phe Leu Trp Lys Leu
```

<210> 411 <211> 51 <212> PRT

```
<213> Homo sapiens
 <220>
 <221> SIGNAL '
 <222> -23..-1
 <400> 411
 Met Ala Phe Gln Ser Leu Leu Glu Met Lys Phe Phe Leu Cys Ala Ala
            -20
                                -15 ·
 Phe Pro Leu Gly Ala Gly Val Lys Met Phe His Tyr Leu Gly Pro Gly
                          1 , . .
                                        5
 Lys Pro Leu Xaa Gln Ala Ser Pro Ser Pro His Pro His Arg Xaa Arg
. 10
            15
Ile Trp Pro
 <210> 412
 <211> 95
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -48..-1 -
 <400> 412
 Met Ala Ser Ser His Trp Asn Glu Thr Thr Thr Ser Val Tyr Gln Tyr
            -45
                                -40
                                                -35
 Leu Gly Phe Gln Val Gln Lys Ile Tyr Pro Phe His Asp Asn Trp Asn
        -30
                            -25
                                                -20
 Thr Ala Cys Phe Val Ile Leu Leu Phe Ile Phe Thr Val Val Ser
                        -10
                                           -5
 Leu Val Val Leu Ala Phe Leu Tyr Glu Val Leu Xaa Xaa Cys Cys
 1
            . 5
                                   10
 Val Lys Asn Lys Thr Val Lys Asp Leu Lys Ser Glu Pro Asn Pro Leu
           20
                               25
 Xaa Xaa Met Met Asp Asn Ile Arg Lys Arg Glu Thr Glu Val Val
 <210> 413
 <211> 60
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -32..-1
 <400> 413
 Met Asp Glu Tyr Ser Trp Trp Cys His Val Leu Glu Val Val Lys Gly
        -30
                            -25
 Gln Met Phe Thr Phe Ile Asn Ile Thr Leu Trp Leu Gly Ser Leu Cys
                         -10
                                            - 5
 Gln Arg Phe Phe Tyr Ala Ser Gly Thr Tyr Phe Leu Ile Tyr Ile Ser
                                    10
```

Thr Val Thr Pro Ser Trp Arg Leu Cys Leu Val Ser

```
<210> 414
<211> 170
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -79..-1
<400> 414
Met Glu Asp Pro Asn Pro Glu Glu Asn Met Lys Gln Gln Asp Ser Pro
             -75
                                  -70
Lys Glu Arg Ser Pro Gln Ser Pro Gly Gly Asn Ile Cys His Leu Gly
          -60
                            -55
Ala Pro Lys Cys Thr Arg Cys Leu Ile Thr Phe Ala Asp Ser Lys Phe
       -45、
                          -40
                                             -35
Gln Glu Arg His Met Lys Arg Glu His Pro Ala Asp Phe Val Ala Gln
                      -25
                                          -20
Lys Leu Gln Gly Val Leu Phe Ile Cys Phe Thr Cys Ala Arg Ser Phe
                   -10
                                      ·-5
Pro Ser Ser Lys Ala Xaa Xaa Thr His Gln Arg Ser His Gly Pro Xaa
                              10
                                               15 ·
Ala Lys Pro Thr Leu Pro Val Ala Thr Thr Ala Gln Pro Thr Phe
Pro Cys Pro Asp Cys Gly Lys Thr Phe Gly Gln Ala Val Ser Leu Xaa
                       40
Arg His Xaa Gln Xaa His Glu Val Arg Ala Pro Pro Gly Thr Phe Ala
           55
                                      60 . '
Cys Thr Xaa Cys Gly Gln Asp Phe Ala Gln Glu Xaa Gly Leu His Gln
                                  75
His Tyr Ile Arg His Ala Arg Gly Gly Leu
<210> 415
```

<210> 415
<211> 190
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -82..-1
<400> 415
Met Tyr Val Trp Pro

Met Tyr Val Trp Pro Cys Ala Val Val Leu Ala Gln Tyr Leu Trp Phe -80 -75 -70 His Arg Arg Ser Leu Pro Gly Lys Ala Ile Leu Glu Ile Gly Ala Gly -60 -55 Val Ser Leu Pro Gly Ile Leu Ala Ala Lys Cys Gly Ala Glu Val Ile -45 Leu Ser Asp Ser Ser Glu Leu Pro His Cys Leu Glu Val Cys Arg Gln -30 -25 Ser Cys Gln Met Asn Asn Leu Pro His Leu Gln Val Val Gly Leu Thr -10 Trp Gly His Ile Ser Trp Asp Leu Leu Ala Leu Pro Pro Gln Asp Ile 10 Ile Leu Ala Ser Asp Val Phe Phe Glu Pro Glu Xaa Phe Glu Asp Ile 20 25 Leu Ala Thr Ile Tyr Phe Leu Met His Lys Asn Pro Lys Val Gln Leu 35

<210> 416 <211> 114 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -60..-1

<400> 416 Met Met Ala Ala Val Pro Pro Gly Leu Glu Pro Trp Asn Arg Val Arg -55 -50 Ile Pro Lys Ala Gly Asn Arg Ser Ala Val Thr Val Gln Asn Pro Gly -40 -35 Ala Ala Leu Asp Leu Cys Ile Ala Ala Val Ile Lys Glu Cys His Leu -25 -20 -15 Val Ile Leu Ser Leu Lys Ser Gln Thr Leu Asp Ala Glu Thr Asp Val -5 Leu Cys Ala Val Leu Tyr Ser Asn His Asn Arg Met Gly Arg His Lys 10 Pro His Leu Ala Leu Lys Gln Val Glu Gln Cys Leu Lys Arg Leu Lys 25 .. 30 Asn Met Asn Leu Glu Gly Ser Ile Gln Asp Leu Phe Glu Leu Phe Ser Ser Lys

<210> 417 <211> 161 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -108..-1

<400> 417 Met Thr Ser Gly Gln Ala Arg Ala Ser Xaa Gln Ser Pro Gln Ala Leu -105 -100 Glu Asp Ser Gly Pro Val Asn Ile Ser Val Ser Ile Thr Leu Thr Leu -85 -80 Asp Pro Leu Lys Pro Phe Gly Gly Tyr Ser Arg Asn Val Thr His Leu -70 Tyr Ser Thr Ile Leu Gly His Gln Ile Gly Leu Ser Gly Arg Glu Ala -55 -50 His Glu Glu Ile Asn Ile Thr Phe Thr Leu Pro Thr Ala Trp Ser Ser -35 Asp Asp Cys Ala Leu His Gly His Cys Glu Gln Val Val Phe Thr Ala -20 Cys Met Thr Leu Thr Ala Ser Pro Gly Val Phe Pro Ser Leu Tyr Ser

```
-10
                             - 5
 His Arg Thr Val Phe Leu Thr Arg Thr Ala Thr Pro Arg Ser Gly Thr
                    10
                                    . 15
 Arg Ser Ser Gln Leu Pro Glu Met Pro Thr Gln Asn Thr Pro Lys Ile
                                     30
 Thr Ile Leu Ser Gly Val Ile Arg Gly Pro Leu Glu Lys Ser Ile Met
                             45
 Leu
           <210> 418
 <211> 67
<212> PRT
<213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -21..-1
 <400> 418
 Met Leu Gly Gly Asp His Arg Ala Leu Leu Leu Lys Ile Trp Leu Leu
                         -15
 Gln Arg Pro Glu Ser Gln Glu Gly Leu Leu Pro Gly Arg Leu Val Val
                                    5
 Met Glu Arg Arg Val Lys Asn Asp Leu Met Ser Phe Leu Ser Thr Val
                                 20
             15
 Leu Leu Ser Phe His Ser Ser Asn Ala Arg Val Ser His Cys Glu Pro
        30
 Leu Arg Met
     45
 <210> 419
 <211> 332
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -32..-1
 <400> 419
 Met Ile Xaa Leu Arg Asp Thr Ala Ala Ser Leu Arg Leu Glu Arg Asp
        -30
                             -25
 Thr Arg Gln Leu Pro Leu Leu Thr Ser Ala Leu His Gly Leu Gln Gln
                         -10
                                             -5
 Gln His Pro Ala Phe Ser Gly Val Ala Arg Leu Ala Lys Arg Trp Val
                                     10
 Arg Ala Gln Leu Leu Gly Glu Gly Phe Ala Asp Glu Ser Leu Asp Leu
 Val Ala Ala Leu Phe Leu His Pro Glu Pro Phe Thr Pro Pro Ser
                             40
 Ser Pro Gln Val Gly Phe Leu Arg Phe Leu Phe Leu Val Ser Thr Phe
 Asp Trp Lys Asn Asn Pro Leu Phe Val Asn Leu Asn Asn Glu Leu Thr
                     70
                                         75
 Val Glu Glu Gln Val Glu Ile Arg Ser Gly Phe Leu Ala Ala Arg Ala
```

90

110

Gln Leu Pro Val Met Val Ile Val Thr Pro Gln Xaa Arg Lys Asn Ser

105

```
Val Trp Thr Glm Asp Gly Pro Ser Ala Glm Ile Leu Glm Glm Leu Val
                          120
                                             125
Val Leu Ala Ala Glu Xaa Leu Pro Met Leu Xaa Xaa Gln Leu Met Asp
                      135
Pro Arg Gly Pro Gly Asp Ile Arg Thr Xaa Phe Arg Pro Pro Leu Asp
                  150
                                     155
Ile Tyr Asp Val Leu Ile Arg Leu Ser Pro Arg His Ile Pro Arg His
               165
                                  170
Arg Gln Ala Val Asp Ser Pro Ala Ala Ser Phe Cys Arg Gly Leu Leu
          180
                              185
                                                 190
Ser Gln Pro Gly Pro Ser Ser Leu Met Pro Val Leu Gly Xaa Asp Pro
        195
                          200
                                             205
Pro Gln Leu Tyr Leu Thr Gln Leu Xaa Glu Ala Phe Gly Asp Leu Ala
                215
Leu Phe Phe Tyr Asp Gln His Gly Glu Val Ile Gly Val Leu Trp
                  230
                                      235
Lys Pro Thr Ser Phe Gln Pro Gln Pro Phe Lys Ala Ser Ser Thr Lys
               245
                                  250
Gly Arg Met Val Met Ser Arg Gly Gly Glu Leu Val Met Val Pro Asn
           260
                              265
Val Glu Ala Ile Leu Glu Asp Phe Ala Val Leu Gly Glu Gly Leu Val
                          280
                               i.
                                             285
Gln Thr Val Glu Ala Arg Ser Glu Arg Trp Thr Val
                       295
```

```
<210> 420
<211> 65
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
```

<222> -19..-1

<210> 421 <211> 57 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -30..-1

-10 Arg Val Tyr His Tyr Phe Gln Trp Arg Arg Ala Gln Arg Gln Ala Ala 10 Glu Glu Gln Lys Xaa Ser Gly Ile Met 25

<210> 422 <211> 85 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -17..-1

65

<400> 422 Met Lys Lys Val Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val -10 -15 Gly Phe Pro Val Ser Gln Asp Gln Glu Arg Glu Lys Arg Ser Ile Ser 10 Asp Ser Asp Glu Leu Ala Ser Gly Xaa Phe Val Phe Pro Tyr Pro Tyr 25 20 Pro Phe Arg Pro Leu Pro Pro Ile Pro Phe Pro Arg Phe Pro Trp Phe 35 40 Arg Arg Asn Phe Pro Ile Pro Ile Pro Glu Ser Ala Pro Thr Thr Pro 50 55 Leu Pro Ser Glu Lys

<210> 423 <211> 85 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -17..-1

<400> 423

Met Lys Lys Val Leu Leu Leu Ile Thr Ala Ile Leu Ala Val Ala Val -15 -10 Gly Phe Pro Val Ser Gln Asp Xaa Glu Arg Glu Lys Arg Ser Ile Ser 10 Asp Ser Asp Glu Leu Ala Ser Gly Phe Phe Val Phe Pro Tyr Pro Tyr 20 25 Pro Phe Arg Pro Leu Pro Pro Ile Pro Phe Pro Arg Phe Pro Trp Phe 40 Arg Arg Asn Phe Pro Ile Pro Ile Pro Glu Ser Ala Pro Thr Thr Pro 50

Leu Pro Ser Glu Lys 65

<210> 424 <211> 69 <212> PRT <213> Homo sapiens

```
١,,,
<220>
<221> SIGNAL
<222> -29..-1
<400> 424
Met Thr Cys Arg Gly Ser Cys Ser Tyr Ala Thr Arg Arg Ser Pro Ser
          ., -25
                     -20 -15
Glu Leu Ser Leu Leu Pro Ser Ser Leu Trp Val Leu Ala Thr Ser Ser
          -10
                            - 5
Pro Thr Ile Thr Ile Ala Leu Ala Met Ala Ala Gly Asn Leu Cys Pro
                    10
                                      15
Leu Pro Ser Ser Xaa Arg Xaa Lys Arg Arg Trp Cys Gln Ala Xaa Gln
           25 30
Gln Xaa Ala Leu Leu
             40
<210> 425
```

<211> 122 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -56..-1

<400> 425 Met Val Pro Trp Pro Arg Gly Lys Val Lys Thr Ala Pro Ile Pro Ile -50 -45 Ser Arg Phe Pro Phe Leu Pro Thr His Asp Pro Pro Thr Pro Ala His -30 -35 . Trp Ser Pro Ala Ser His Gln Gln Phe Lys His Xaa Ser Pro Leu Leu -15 Thr Leu Ala Leu Leu Gly Gln Cys Ser Leu Phe Xaa Asn Leu Arg Lys Lys Leu Ala Gly Gln Lys Ala Lys Lys Leu Pro Ser Phe Ser Ser Leu 15 Pro Leu Thr Leu Trp Pro Leu Thr Pro Gln Phe Ala Glu Leu Thr Thr 30 35 Val Ala Gln Lys Lys Leu Arg Trp Ser Gly Thr Leu Gly Trp Gly Pro 45 50 Val Pro Ser Trp Val Gln Phe Phe Leu Gly 60

<210> 426 <211> 41 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -30..-1

Met Ala Cys Glu Thr His Gly Val Leu Val Pro Ala His Leu Ser Gly
-30 -25 -20 -15
Leu Ile Thr Cys Leu Leu Ala Phe Trp Val Pro Ala Ser Cys Ile Gln
-10 -5 1

Arg Cys Ser Gly Ser Pro Leu Pro Leu 5

<210> 427 <211> 50 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -36..-1

. <400> 427

<210> 428
<211> 136
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> -18..-1

<400> 428

Met Asp Ser Leu Arg Lys Met Leu Ile Ser Val Ala Met Leu Gly Ala -10 -15 Xaa Ala Gly Val Gly Tyr Ala Leu Leu Val Ile Val Thr Pro Gly Glu 10 Arg Arg Lys Gln Glu Met Leu Lys Glu Met Pro Leu Gln Asp Pro Arg 20 25 Ser Arg Glu Glu Ala Ala Arg Thr Gln Gln Leu Leu Ala Thr Leu 40 35 Gln Glu Ala Ala Thr Thr Gln Glu Asn Val Ala Trp Arg Lys Asn Trp 55 Met Val Gly Gly Gly Gly Ala Thr Gly Xaa His Arg Glu Thr Gly 70 Leu Ala Ser Val Gly Ala Gly Pro Trp Leu Gly Arg Arg Asn Pro Arg 85 Gln Leu Ser Pro Ser Trp Ala Xaa Arg Lys Ile Arg Xaa Glu Asn Xaa 105 100 Met Pro Gly Leu Ser Gly Val Leu 115

<210> 429 <211> 194 <212> PRT <213> Homo sapiens

<220>

<221> SIGNAL " <222> -65..-1

<400> 429

Met Gln Asp Ala Pro Leu Ser Cys Leu Ser Pro Thr Lys Trp Ser Ser -60 -55 Val Ser Ser Ala Asp Ser Thr Glu Lys Ser Ala Ser Ala Ala Gly Thr -45 -40 Arg Asn Leu Pro Phe Gln Phe Cys Leu Arg Gln Ala Leu Arg Met Lys -25 Ala Ala Gly Ile Leu Thr Leu Ile Gly Cys Leu Val Thr Gly Val Glu Ser Lys Ile Tyr Thr Arg Cys Lys Leu Ala Lys Ile Phe Ser Arg Ala 10 Gly Leu Asp Asn Xaa Arg Gly Phe Ser Leu Gly Asn Trp Ile Cys Met 25 Ala Tyr Tyr Glu Ser Gly Tyr Asn Thr Thr Ala Gln Thr Val Leu Asp 40 Asp Gly Ser Ile Asp Tyr Gly Ile Phe Gln Ile Asn Ser Phe Ala Trp 55 Cys Arg Arg Gly Lys Leu Lys Glu Asn Asn His Cys His Val Ala Cys 70 Ser Ala Leu Xaa Thr Asp Asp Leu Thr Asp Ala Ile Ile Cys Ala Xaa 90 Lys Ile Val Lys Glu Thr Gln Gly Met Asn Tyr Trp Gln Gly Trp Lys 100 105 Lys His Cys Glu Gly Arg Asp Leu Ser Xaa Trp Lys Lys Gly Cys Glu 120

<210> 430 <211> 141

Val Ser

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -69..-1

<400> 430

Met Thr Ser Gln Pro Val Pro Asn Glu Thr Ile Ile Val Leu Pro Ser Asn Val Ile Asn Phe Ser Gln Ala Glu Lys Pro Glu Pro Thr Asn Gln -50 -45 Gly Gln Asp Ser Leu Lys Lys His Leu His Ala Glu Ile Lys Val Ile -30 Gly Thr Ile Gln Ile Leu Cys Gly Met Met Val Leu Ser Leu Gly Ile -15 -10 Ile Leu Ala Ser Ala Ser Phe Ser Pro Asn Phe Thr Gln Val Thr Ser Thr Leu Leu Asn Ser Ala Tyr Pro Phe Ile Gly Pro Phe Phe Val Xaa 20 Lys Xaa Ser Glu Glu Gly Arg Met Gly Gln Xaa Gly Glu Glu Xaa Xaa 35 Asn Ser Leu Asn Phe Pro Xaa Ala Ser Leu Leu Xaa Leu Ile Cys Gln

Xaa Gln Gly Phe Asn Gly Glu Ser Cys Ser Pro Val Gly

```
<210> 431
 <211> 248
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -69..-1
 <400> 431
 Met Thr Ser Gln Pro Val Pro Asn Glu Thr Ile Ile Val Leu Pro Ser
                -65
                                     -60
Asn Val Ile Asn Phe Ser Gln Ala Glu Lys Pro Glu Pro Thr Asn Gln
             -50
                                 -45
 Gly Gln Asp Ser Leu Lys Lys His Leu His Ala Glu Xaa Lys Val Ile
        -35 🕟
                             -30
 Gly Thr Ile Gln Ile Leu Cys Gly Met Met Val Leu Ser Leu Gly Ile
                         -15
                                             -10
 Ile Leu Ala Ser Ala Ser Phe Ser Pro Asn Phe Thr Gln Val Thr Ser
 Thr Leu Leu Asn Ser Ala Tyr Pro Phe Ile Gly Pro Phe Phe Phe Ile
             15
                                 20
 Ile Ser Gly Ser Leu Ser Ile Ala Thr Lys Lys Arg Leu Thr Asn Leu
                             35
 Leu Val His Thr Thr Leu Val Gly Ser Ile Leu Ser Ala Leu Ser Ala
 Leu Val Gly Phe Ile Xaa Leu Ser Val Lys Gln Ala Thr Leu Asn Pro
                                         70 .
                     65
 Ala Ser Leu Xaa Cys Glu Leu Xaa Lys Asn Asn Ile Pro Thr Xaa Xaa
                 80
                                     85
                                                         90
 Tyr Val Xaa Tyr Phe Tyr His Asp Ser Leu Tyr Thr Thr Asp Xaa Tyr
                                 100
 Thr Ala Lys Ala Xaa Leu Ala Gly Thr Leu Ser Leu Met Leu Ile Cys
                                                 120
         110
                             115
 Thr Leu Leu Glu Phe Cys Xaa Xaa Val Leu Thr Ala Val Leu Arg Trp
                         130
 Lys Gln Ala Tyr Ser Asp Phe Pro Gly Ser Val Leu Phe Leu Pro Xaa
                     145
                                        150
 Ser Tyr Ile Gly Asn Ser Gly Met Ser Ser Lys Met Thr His Asp Cys
                 160
                                     165
 Gly Tyr Glu Glu Leu Leu Thr Ser
             175
```

Phe

<210> 433
<211> 86
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL

<400> 433

<222> -14..-1

Met Val Ala Leu Asn Leu Ile Leu Val Pro Cys Cys Ala Ala Trp Cys -10 -5 Asp Pro Arg Arg Ile His Ser Gln Asp Asp Val Leu Arg Ser Ser Ala 10 Ala Asp Thr Gly Ser Ala Met Gln Arg Arg Glu Ala Trp Ala Gly Trp 25 30 Arg Arg Ser Gln Pro Phe Ser Val Gly Leu Pro Ser Ala Glu Arg Leu 40 45· Glu Asn Gln Pro Gly Lys Leu Ser Trp Arg Ser Leu Val Gly Glu Gly 55 60 His Arg Ile Cys Asp Leu 70

<210> 434 <211> 144 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -58..-1

<400> 434 Met Thr Arg Leu Cys Leu Pro Arg Pro Glu Ala Arg Glu Asp Pro Ile -50 Pro Val Pro Pro Arg Gly Leu Gly Ala Gly Glu Gly Ser Gly Ser Pro -35 Val Arg Pro Pro Val Ser Thr Trp Gly Pro Ser Trp Ala Gln Leu Leu -20 -15 Asp Ser Val Leu Trp Leu Gly Ala Leu Gly Leu Thr Ile Gln Ala Val - 5 Phe Ser Thr Thr Gly Pro Ala Leu Leu Leu Leu Leu Val Ser Phe Leu Thr Phe Asp Leu Leu His Arg Pro Ala Val Thr Leu Cys His Ser Ala 30 Asn Phe Ser Pro Gly Ala Arg Val Arg Gly Pro Val Lys Val Leu Asp Ser Arg Arg Leu Tyr Ser Cys Lys Trp Val Gln Ser Gln Asp Asn Leu 65 Ala Ser Arg Lys His Cys Cys Cys Cys Ser Trp Gly Trp Ala Arg Ser 75 . 80

```
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 435
Met Glu Arg Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala
                        -10
Ser Ala Gly Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln
Cys Phe Lys Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser
                                25
Pro Leu Asp Gln Val Cys Ile Ser Asn Glu Val Val Val Ser Phe Ser
Glu Ser Pro Pro Gly Arg Gly Xaa Val Pro Xaa Ala Gly Glu Xaa Pro
                        55
Val Pro Pro Pro Leu Xaa Asp Leu Xaa Met Thr Pro Arg Xaa Xaa Arg
                    70
                                  . 75
Ala Trp Gly Pro Val Gly Pro Lys Val Pro Pro Ala Val Ser Pro Ala
                85
                                   90
Leu Gly Ser Gly Glu His Pro Xaa Xaa
            100
```

<210> 436 <211> 162 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<222> -16..-1

<400> 436

145

<212> PRT

Met Glu Arg Leu Val Leu Thr Leu Cys Thr Leu Pro Leu Ala Val Ala -10 Ser Ala Gly Cys Ala Thr Thr Pro Ala Arg Asn Leu Ser Cys Tyr Gln Cys Phe Lys Val Ser Ser Trp Thr Glu Cys Pro Pro Thr Trp Cys Ser 25 Pro Leu Asp Gln Val Cys Ile Ser Asn Glu Val Val Val Ser Phe Lys 40 Trp Ser Val Arg Val Leu Leu Ser Lys Arg Cys Ala Pro Arg Cys Pro Asn Asp Asn Met Xaa Phe Glu Trp Ser Pro Ala Pro Met Val Gln Gly 70 75 Val Ile Thr Arg Arg Cys Cys Ser Trp Ala Leu Cys Asn Arg Ala Leu Thr Pro Gln Glu Gly Arg Trp Ala Leu Xaa Gly Gly Leu Leu Leu Gln 105 Asp Pro Ser Arg Gly Xaa Lys Thr Trp Val Arg Pro Gln Leu Gly Leu 120 Pro Leu Cys Leu Pro Xaa Ser Asn Pro Leu Cys Pro Xaa Glu Thr Gln 130 135 Glu Gly

```
<210> 437
<211> 110
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
<400> 437
Met Xaa Leu Met Val Leu Val Phe Thr Ile Gly Leu Thr Leu Leu Leu
                           ·· -10
                   -15
Gly Xaa Gln Ala Met Pro Ala Asn Arg Leu Ser Cys Tyr Arg Lys Ile
               1 "...
Leu Lys Asp His Asn Cys His Asn Leu Pro Glu Gly Val Ala Asp Leu
                           20
Thr Gln Ile Asp Val Asn Val Gln Asp His Phe Trp Asp Gly Lys Gly
                                           40
Cys Glu Met Ile Cys Tyr Cys Asn Phe Lys Arg Ile Ala Leu Leu Pro
            ·· 50
                                    . '55
Lys Arg Arg Phe Leu Trp Thr Lys Asp Leu Phe Arg Asp Ser Leu Gln
               65
                                  70 ··
Gln Ser Met Arg Ile Phe Met Tyr Ser Gly Glu His His Ser
            80
                               85
<210> 438
<211> 71
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 438
Met Lys Leu Leu Thr His Asn Leu Leu Ser Ser His Val Arg Gly Val
                                       -5
Gly Ser Arg Gly Phe Pro Leu Arg Leu Gln Ala Thr Glu Val Arg Ile
                               10
Cys Pro Val Glu Phe Asn Pro Asn Phe Val Ala Arg Met Ile Pro Lys
                           25
Val Glu Trp Ser Ala Phe Leu Glu Ala Xaa Asp Asn Leu Arg Leu Ile
Gln Val Pro Arg Arg Ala Gly
<210> 439
<211> 99
<212> PRT
<213> Homo sapiens
<220>
```

<400> 439

<221> SIGNAL <222> -24..-1

Met Lys Ser Ala Lys Leu Gly Phe Leu Leu Arg Phe Phe Ile Phe Cys
-20 -15 -10

 Ser
 Leu
 Asn
 Thr
 Leu
 Leu
 Leu
 Gly
 Gly
 Val
 Asn
 Lys
 Ile
 Ala
 Glu
 Lys

 Ile
 Cys
 Gly
 Asp
 Leu
 Lys
 Asp
 Pro
 Cys
 Lys
 Leu
 Asp
 Met
 Asn
 Phe
 Gly

 Ser
 Cys
 Tyr
 Glu
 Val
 His
 Phe
 Arg
 Tyr
 Phe
 Tyr
 Asn
 Arg
 Thr
 Ser
 Lys

 25
 Tyr
 Glu
 Tyr
 Phe
 Val
 Asn
 Gly
 Asn
 Leu
 Asn
 Asn
 Asn

 Arg
 Cys
 Glu
 Tyr
 Phe
 Val
 Asn
 Gly
 Asn
 Leu
 Asn
 Asn
 Asn

 Phe
 Lys
 Leu
 Lys
 Ile
 Glu
 Arg
 Glu
 Val
 Xaa
 Cys
 Val
 Ala
 Lys
 Tyr
 Lys

 Phe
 Lys
 Lys
 Lys
 Lys
 Lys
 Lys
 Lys
 Lys
 Lys
 Ly

<210> 440
<211> 169
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1

100

1!

Leu Leu Thr Pro Thr Trp Lys Ala Glu Thr Thr Cys Arg Leu Arg Ala
25 30 35

Thr His Gly Cys Arg Asn Pro Thr Leu Val Gln Leu Asp Gln Tyr Glu 40 50 55 Asn His Gly Leu Val Pro Asp Gly Ala Val Cys Ser Asn Leu Pro Tyr

Asn His Gly Leu Val Pro Asp Gly Ala Val Cys Ser Asn Leu Pro Tyr
60 65 70

Ala Ser Trp Phe Glu Ser Phe Cys Gln Phe Thr His Tyr Arg Cys Ser 75 80 85

Asn His Val Tyr Tyr Ala Lys Arg Val Leu Cys Ser Gln Pro Val Ser 90 95 100

Ile Leu Ser Pro Asn Thr Leu Lys Glu Ile Glu Xaa Ser Ala Glu Val 105 110 115

Ser Pro Thr Thr Asp Asp Leu Pro His Leu Thr Pro Leu His Ser Asp 120 125 130 135

Arg Thr Pro Asp Leu Pro Ala Leu Ala

140

<210> 441 <211> 167 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -76..-1

Ala Asp Cys Gly Thr Ile Leu Leu Gln Asp Lys Gln Arg Lys Ile Tyr -55 -50 Cys Val Ala Cys Gln Glu Leu Asp Ser Asp Val Asp Lys Asp Asn Pro -40 -35 Ala Leu Asn Ala Gln Ala Ala Leu Ser Gln Ala Arg Glu His Gln Leu -20 Ala Ser Ala Ser Glu Leu Pro Leu Gly Ser Arg Pro Ala Pro Gln Pro Pro Val Pro Arg Pro Glu His Cys Glu Gly Ala Ala Ala Gly Leu Lys 10 15. Ala Ala Gln Gly Pro Pro Ala Pro Ala Val Pro Pro Asn Thr Xaa Val 25 30 Met Ala Cys Thr Gln Thr Ala Leu Leu Gln Lys Leu Thr Trp Ala Ser 45 Ala Glu Leu Gly Ser Xaa Thr Ser Xaa Gly Lys Xaa Ala Ser Ser Cys 60 Val Ala Leu Ser Ala His Val Arg Arg Pro Cys Ala Ala Cys Ser Ser 75 Tyr Ser Thr Lys Arg Ser Pro 90

<210> 442 <211> 70 <212> PRT

<213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

<400> 442

 Met Ile Leu Cys Phe Leu Leu Pro His His Arg Leu Gln Glu Ala Arg

 -15
 -10
 -5
 1

 Gln Ile Gln Val Leu Lys Met Leu Pro Arg Glu Lys Leu Arg Arg
 15
 15

 Glu Glu Arg Lys Gln Ile Asn Gly Lys Lys Xaa Arg Thr Lys Tyr Glu
 20
 25

 Thr Pro Arg Lys Xaa Xaa Gly Lys Lys Gly Gly Asn Xaa Xaa Xaa Xaa
 35
 40

Xaa Leu Ser Lys Arg Asp 50 55

<210> 443

<211> 381

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -33..-1

<400> 443

Met Ser Trp Thr Val Pro Val Val Arg Ala Ser Gln Arg Val Ser Ser -30 -25 -20

Val Gly Ala Asn Xaa Leu Cys Leu Gly Met Ala Leu Cys Pro Arg Gln
-15 -10 -5

Ala Thr Arg Ile Pro Leu Asn Gly Thr Trp Leu Phe Thr Pro Val Ser

Lys Met Ala Thr Val Lys Ser Glu Leu Ile Glu Arg Phe Thr Ser Glu , 20 Lys Pro Val His His Ser Lys Val Ser Ile Ile Gly Thr Gly Ser Val 40 Gly Met Ala Cys Ala Ile Ser Ile Leu Leu Lys Gly Leu Ser Asp Glu . 55 Leu Ala Leu Val Asp Leu Asp Glu Xaa Lys Leu Lys Gly Glu Thr Met 70 Asp Leu Gln His Gly Ser Pro Phe Thr Lys Met Pro Asn Ile Val Cys 85 90 Ser Lys Xaa Tyr Phe Val Thr Ala Asn Ser Asn Leu Val Ile Ile Thr 100 Ala Gly Ala Arg Gln Xaa Lys Gly Glu Thr Arg Leu Asn Leu Xaa Gln .120 Arg Asn Val Ala Ile Phe Lys Leu Met Ile Ser Ser Ile Val Gln Tyr 135 Ser Pro His Cys Lys Leu Ile Ile Val Ser Asn Pro Val Asp Ile Leu 155 150 Thr Tyr Val Ala Trp Lys Leu Ser Ala Phe Pro Lys Asn Arg Ile Ile 165 170 Gly Ser Gly Cys Asn Leu Ile Xaa Ala Arg Phe Arg Phe Leu Ile Gly 180 185 Gln Lys Leu Gly Ile His Ser Glu Ser Cys His Gly Trp Ile Leu Gly 195 200 Glu His Gly Asp Ser Ser Val Pro Val Trp Ser Gly Val Asn Ile Ala 215 Gly Val Pro Leu Lys Asp Leu Asn Ser Asp Ile Gly Thr Asp Lys Asp 230 235 Pro Glu Gln Trp Lys Asn Val His Lys Glu Val Thr Ala Thr Ala Tyr 250 245 Glu Ile Ile Lys Met Lys Gly Tyr Thr Ser Trp Ala Ile Gly Leu Ser 265 260 Val Ala Asp Leu Thr Glu Ser Ile Leu Lys Asn Leu Arg Arg Ile His 280 275 Pro Val Ser Thr Ile Thr Lys Gly Leu Tyr Gly Ile Xaa Glu Glu Val 295 Phe Leu Ser Ile Pro Cys Ile Leu Gly Glu Asn Gly Ile Thr Asn Leu 315 310 Ile Lys Ile Lys Leu Thr Pro Glu Glu Glu Ala His Leu Lys Lys Ser 325 Ala Lys Thr Leu Trp Glu Ile Gln Asn Lys Leu Lys Leu 340

<210> 444 <211> 39 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -14..-1

```
<210> 445
 <211> 50
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL.
 <222> -37..+1
 <400> 445
Met Val Leu Thr Thr Leu Pro Leu Pro Ser Ala Asn Ser Pro Val Asn
                         -30
                                              -25
 Met Pro Thr Thr Gly Pro Asn Ser Leu Ser Tyr Ala Ser Ser Ala Leu
                         -15
                                             -10
 Ser Pro Cys Leu Thr Ala Pro Lys Ser Pro Arg Leu Ala Met Met Pro
 - 5
                                     5
 Asp Asn
 <210> 446
 <211> 51
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -26..-1
 <400> 446
 Met Thr Pro Trp Cys Leu Ala Cys Leu Gly Arg Arg Pro Leu Ala Ser
 Leu Gln Trp Ser Leu Thr Leu Ala Trp Cys Gly Ser Gly Ser His Trp
                     -5
 Thr Glu Arg Pro Xaa Gln Xaa Ser Pro Trp Xaa Ser Leu Ser Ala Thr
                                 15
 Thr Arg Gly
         25
 <210> 447
 <211> 242
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -30..-1
 <400> 447
 Met Gly Glu Ala Ser Pro Pro Ala Pro Ala Arg Arg His Leu Leu Val
                     -25
 Leu Leu Leu Leu Ser Thr Leu Val Ile Pro Ser Ala Ala Ala Pro
 Ile His Asp Ala Asp Ala Gln Glu Ser Ser Leu Gly Leu Thr Gly Leu
                              10
 Gln Ser Leu Leu Gln Gly Phe Ser Arg Leu Phe Leu Lys Gly Asn Leu
                          25
```

Leu Arg Gly Ile Asp Ser Leu Phe Ser Ala Pro Met Asp Phe Arg Gly

40 Leu Pro Gly Asn Tyr His Lys Glu Glu Asn Gln Glu His Gln Leu Gly 55 60 Asn Asn Thr Leu Ser Ser His Leu Gln Ile Asp Lys Met Thr Asp Asn 70 75 Lys Thr Gly Glu Val Leu Ile Ser Glu Asn Val Val Ala Ser Ile Gln 90 Pro Xaa Glu Gly Xaa Phe Glu Gly Asp Leu Lys Val Pro Arg Met Glu 105 Glu Lys Glu Ala Leu Val Pro Xaa Gln Lys Ala Thr Asp Ser Phe His 120 125 Thr Glu Leu His Pro Arg Val Ala Phe Trp Ile Ile Lys Leu Pro Arg 135 140 Arg Arg Ser His Gln Asp Ala Leu Glu Gly Gly His Trp Leu Xaa Glu 150 155 Lys Arg His Arg Leu Gln Ala Ile Arg Asp Gly Leu Arg Lys Gly Thr 170 His Lys Asp Xaa Leu Xaa Xaa Gly Thr Glu Ser Ser His Ser Arg 185 190 Leu Ser Pro Arg Lys Xaa His Leu Leu Tyr Ile Leu Xaa Pro Ser Arg 205 195 200 Gln Leu

<210> 448
<211> 154
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL

<400> 448

<222> -60..-1

Met Gly Ser Lys Cys Cys Lys Gly Gly Pro Asp Glu Asp Ala Val Glu -55 -50 Arg Gln Arg Arg Gln Lys Leu Leu Ala Gln Leu His His Arg Lys -35 Arg Val Lys Ala Ala Gly Gln Ile Gln Ala Trp Trp Arg Gly Val Leu -20 Val Arg Arg Thr Leu Leu Val Ala Ala Leu Arg Ala Trp Met Ile Gln -5 Cys Trp Trp Arg Thr Leu Val Gln Arg Arg Ile Arg Gln Arg Arg Gln 10 Ala Leu Leu Gly Val Tyr Val Ile Gln Glu Gln Ala Ala Val Lys Leu 25 30 Gln Ser Cys Ile Arg Met Trp Gln Cys Arg Gln Cys Tyr Arg Gln Met 45 Cys Asn Ala Leu Cys Leu Phe Gln Val Pro Lys Ser Ser Leu Ala Phe 60 Gln Thr Asp Gly Phe Leu Gln Val Gln Tyr Ala Ile Pro Ser Lys Gln 75 Pro Glu Phe His Ile Glu Ile Leu Ser Ile

<210> 449 <211> 89

<212> PRT

<213> Homo sapiens

Ala Ile Ile Leu Met Lys

```
<220>
<221> SIGNAL
<222> -61..-1
<400> 449
Met Asn Ala Ala Ile Asn Thr Gly Pro Ala Pro Ala Val Thr Lys Thr
                      -55
                            -50
Glu Thr Glu Val Gln Asn Pro Asp Val Leu Trp Asp Leu Asp Ile Pro
                  -40
                           / -35
Glu Ala Arg Ser' His Ala Asp Gln Asp Ser Asn Pro Lys Ala Glu Ala
              -25
                                ~20
Leu Leu Pro Cys Asn Leu His Cys Ser Trp Leu His Ser Ser Pro Arg
           -10 -5
Pro Asp Pro His Ser His Phe Pro Ser Xaa Arg Arg Cys Pro Leu Pro
                      10
                                         15
His Pro Cys Ala Thr Tyr Pro Pro Xaa
                   25
<210> 450
<211> 73
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1 ' '
<400> 450
Met Arg Met Ser Leu Ala Gln Arg Val Leu Leu Thr Trp Leu Phe Thr
                      -20
                            -15
Leu Leu Phe Leu Ile Met Leu Val Leu Lys Leu Asp Glu Lys Ala Pro
                  -5
Trp Asn Trp Phe Leu Ile Phe Ile Pro Val Trp Ile Phe Asp Thr Ile
          10
Leu Leu Val Leu Leu Ile Val Lys Met Ala Gly Arg Cys Lys Ser Gly
                          30
Phe Asp Leu Asp Met Asp His Thr Ile
<210> 451
<211> 54
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -34..-1
<400> 451
Met Ile Pro Leu Ile Ser His Leu Ala Glu Ala Ala Pro Pro Thr Ser
               -30
                                  -25
Trp Ser Leu Ile Ser Ser Val Leu Asn Val Gly His Leu Leu Phe Ser
                              -10
Ser Ala Cys Ser Val Ser Leu Glu Ala Leu Ser Thr Arg Asn Ile Lys
```

```
<210> 452
 <211> 121
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -38..-1
 <400> 452
Met Glu Ser Pro Gln Leu His Cys Ile Leu Asn Ser Asn Ser Val Ala
                                 -30
             -35
 Cys Ser Phe Ala Val Gly Ala Gly Phe Leu Ala Phe Leu Ser Cys Leu
      -20 \
                            -15
                                                -10
 Ala Phe Leu Val Leu Asp Thr Gln Glu Thr Arg Ile Ala Gly Thr Arg
                        1
 Phe Lys Thr Ala Phe Gln Leu Leu Asp Phe Ile Leu Ala Val Leu Trp
                                    20
 Ala Val Val Trp Phe Met Gly Phe Cys Phe Leu Ala Asn Gln Trp Gln
             30
                                 35
 His Ser Pro Pro Lys Glu Xaa Leu Leu Gly Ser Ser Ser Ala Gln Ala
 Ala Ile Gly Xaa His Leu Leu His Pro Cys Leu Asp Ile Pro Xaa
 Leu Pro Gly Xaa Pro Gly Pro Pro Lys
                     80
 <210> 453
 <211> 166
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -37..-1
 <400> 453
 Met Ser Thr Val Gly Leu Phe His Phe Pro Thr Pro Leu Thr Arg Ile
                             -30
 Cys Pro Ala Pro Trp Gly Leu Arg Leu Trp Glu Lys Leu Thr Leu Leu
                         -15
                                             -10
 Ser Pro Gly Ile Ala Val Thr Pro Val Gln Met Ala Gly Lys Lys Asp
 Tyr Pro Ala Leu Leu Ser Leu Asp Glu Asn Glu Leu Glu Glu Gln Phe
                                 20
 Val Lys Gly His Gly Pro Gly Gly Gln Ala Thr Asn Lys Thr Ser Asn
                             35
 Cys Val Val Leu Lys Xaa Ile Pro Ser Gly Ile Val Val Lys Cys His
                         50
 Gln Thr Arg Ser Val Asp Gln Asn Arg Lys Leu Ala Arg Lys Ile Leu
                     65
                                         70
 Gln Glu Lys Val Xaa Val Phe Tyr Asn Gly Glu Asn Ser Pro Val His
                                     85
```

Lys Glu Lys Arg Glu Ala Ala Lys Lys Lys Gln Glu Arg Lys Lys Arg
95 100 105

Ala Lys Glu Thr Leu Glu Lys Lys Xaa Leu Leu Lys Xaa Leu Trp Glu
110 115 120

Ser Ser Lys Lys Val His 125

<210> 454
<211> 180
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1

<400> 454 Met Gly Ile Gln Thr Ser Pro Val Leu Leu Ala Ser Leu Gly Val Gly -20 Leu Val Thr Leu Leu Gly Leu Ala Val Gly Ser Tyr Leu Val Arg Arg - 5 Ser Arg Arg Pro Gln Val Thr Leu Leu Asp Pro Asn Glu Lys Tyr Leu 10 15 Leu Arg Leu Leu Asp Lys Thr Thr Val Ser His Asn Thr Lys Arg Phe 30 Arg Phe Ala Leu Pro Thr Ala His His Thr Leu Gly Leu Pro Val Gly 45 Lys His Ile Tyr Leu Ser Thr Arg Ile Asp Gly Ser Leu Val Ile Arg 60 65 Pro Tyr Thr Pro Val Thr Ser Asp Glu Asp Gln Gly Tyr Val Asp Leu 75 Val Xaa Lys Val Tyr Leu Lys Gly Val His Pro Lys Phe Pro Glu Gly 90 Gly Lys Met Ser Xaa Tyr Leu Asp Xaa Leu Lys Val Gly Asp Xaa Val 110 115 Glu Phe Xaa Gly Pro Ser Gly Leu Leu Thr Tyr Thr Gly Lys Gly His 125 130 Phe Asn Ile Gln Pro Asn Lys Asn Leu His Gln Asn Pro Glu Trp Arg

<210> 455
<211> 91
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -64..-1
<400> 455

Arg Asn Trp Glu

20 25

```
<210> 456
<211> 257
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
```

<400> 456

```
Met Arg Arg Ile Ser Leu Thr Ser Ser Pro Val Arg Leu Leu Xaa
          -20
                               -15
Leu Leu Leu Leu Ile Ala Leu Glu Ile Met Val Gly Gly His Ser
Leu Cys Phe Asn Phe Thr Ile Lys Ser Leu Ser Arg Pro Gly Gln Pro
Trp Cys Glu Ala His Val Phe Leu Asn Lys Asn Leu Phe Leu Gln Tyr
               30
                                   35
Asn Ser Asp Asn Asn Met Val Lys Pro Leu Gly Leu Leu Gly Lys Lys
           45
Val Tyr Ala Thr Ser Thr Trp Gly Glu Leu Thr Gln Thr Leu Gly Glu
Val Gly Arg Asp Leu Arg Met Leu Leu Cys Asp Ile Lys Pro Gln Ile
                       80
Lys Thr Ser Asp Pro Ser Thr Leu Gln Val Xaa Xaa Phe Cys Gln Arg
                   95
                                       100
Glu Ala Glu Arg Cys Thr Gly Ala Ser Trp Gln Phe Ala Thr Asn Gly
               110
                                   115
Glu Lys Ser Leu Leu Phe Asp Ala Met Asn Met Thr Trp Thr Val Ile
                               130
Asn His Glu Ala Ser Xaa Ile Lys Glu Thr Trp Lys Lys Asp Arg Xaa
                           145
                                               150
Leu Glu Xaa Tyr Phe Arg Lys Leu Ser Lys Gly Asp Cys Asp His Trp
                       160
Leu Arg Glu Phe Leu Gly His Trp Glu Ala Met Pro Xaa Pro Xaa Val
                   175
                                       180
Ser Pro Xaa Asn Ala Ser Xaa Ile His Trp Ser Ser Ser Xaa Leu Pro
               190
                                   195
Xaa Xaa Trp Ile Ile Leu Gly Ala Phe Ile Leu Leu Xaa Leu Met Gly
Ile Val Leu Ile Cys Val Trp Trp Gln Asn Gly Xaa Xaa Ser Thr Xaa
                            225
```

```
<210> 457
<211> 193
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -60..-1
<400> 457
Met Cys Pro Ser Leu Glu Glu Ala Pro Ser Val Lys Gly Thr Leu Pro
```

-55

-50

Xaa

Cys Ser Gly Gin Gln Pro Phe Pro Phe Gly Ala Ser Asn Ile Pro " **-4**0 -35 Leu Leu Cly Arg Ser Arg Lys Val Ala Arg Gly Ala Pro Val Leu -20 Trp Pro Phe Leu Thr Trp Ile Asn Pro Ala Leu Ser Ile Cys Asp Pro Leu Gly Ser Cys Gly Trp Xaa Cys His Thr Ala Gln Val Pro Ala Pro 10 15 Leu Gln Leu Pro Thr Ala Cys Pro Pro Leu Pro His Gly Thr Arg Ala .. 25 30 Val Gly Pro Thr Pro Gly Leu Leu Pro Glu Ala Ala Pro Xaa Thr 45 Xaa Gly Ala Leu Ser Ser Arg Ser Arg His Trp Ser Cys Ser Ile Val 55 60 Xaa Cys Leu His Leu His Xaa Leu Leu Ser Val Glu Thr Arg Xaa Phe 75 Xaa Lys His Leu Leu Val Leu Val Ala Val Ala His Ser Val Leu 90 95 Glu Pro Pro Ala Leu Val Pro Asn Val Gln Cys Glu Met Cys Thr His 105 Ser Gly Pro Arg Asp Leu Glu Ala Ala Val Val Ser Pro Ala Pro Trp 120 125 Glu

<210> 458 <211> 107 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -28..-1

<400> 458

Met Val Leu Thr Leu Gly Glu Ser Trp Pro Val Leu Val Gly Arg Arg -20 Phe Leu Ser Leu Ser Ala Ala Asp Gly Ser Asp Gly Ser His Asp Ser -10 ~5 Trp Asp Val Glu Arg Val Ala Glu Trp Pro Trp Leu Ser Gly Thr Ile 10 15 Arg Ala Val Ser His Thr Asp Val Thr Lys Lys Asp Leu Lys Val Cys 25 30 Val Glu Phe Xaa Gly Glu Ser Trp Arg Lys Arg Arg Trp Ile Glu Val 45 Tyr Ser Leu Leu Arg Lys Ala Phe Leu Val Lys His Asn Leu Val Leu Ala Glu Arg Lys Ser Pro Glu Ile Ser Trp Gly

<210> 459 <211> 121 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -13..-1

<400> 459 Met Leu Val Leu Arg Ser Ala Leu Thr Arg Ala Leu Ala Ser Arg Thr -10 -5 Leu Ala Pro Gln Met Cys Ser Ser Phe Ala Thr Gly Pro Arg Gln Tyr 10 15 Asp Gly Ile Phe Tyr Glu Phe Arg Ser Tyr Tyr Leu Lys Pro Ser Lys 30 Met Asn Glu Phe Leu Glu Asn Phe Glu Lys Asn Ala Gln Leu Arg Thr 45 Ala His Ser Glu Leu Val Gly Tyr Trp Ser Val Xaa Phe Gly Gly Arg ` <sup>;</sup>'55 60 Met Xaa Thr Val Phe His Ile Trp Lys Tyr Asp Asn Phe Ala His Arg Thr Glu Phe Gln Lys Ala Leu Ala Lys Asp Lys Glu Trp Gln Glu Gln 90 Phe Leu Ile Pro Asn Leu Ala Leu Asn 105

<210> 460 <211> 44 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -17..-1

<210> 461 <211> 109 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -13..-1

85

90

95

```
<210> 462
<211> 143
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -41..-1
<400> 462
Met Ala Thr Ala Thr Glu Gln Trp Val Leu Val Glu Met Val Gln Ala
                       -35
                                    ~30
Leu Tyr Glu Ala Pro Ala Tyr His Leu Ile Leu Glu Gly Ile Leu Ile
                    -20
Leu Trp Ile Ile Arg Leu Leu Phe Ser Lys Thr Tyr Lys Leu Gln Glu
                               1
Arg Ser Asp Leu Thr Val Lys Glu Lys Glu Glu Leu Ile Glu Glu Trp
                           15
Gln Pro Glu Pro Leu Val Pro Pro Val Pro Lys Asp His Pro Ala Leu
                       30
Asn Tyr Asn Ile Val Ser Gly Pro Pro Ser His Lys Thr Val Val Asn
                    45
                                       50
Gly Lys Glu Cys Ile Asn Phe Ala Ser Phe Asn Phe Leu Gly Leu Leu
                                   65.
Asp Asn Pro Arg Val Lys Ala Ala Ala Leu Ala Ser Leu Lys Lys Tyr
                               80
Gly Val Gly Thr Cys Gly Pro Cys Gly Phe Tyr Gly Thr Phe Glu
                          95
```

<210> 463 <211> 232 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<400> 463

<222> -30..-1

Met Ala Ala Thr Ser Gly Thr Asp Glu Pro Val Ser Gly Glu Leu Val -25 -20 Ser Val Ala His Ala Leu Ser Leu Pro Ala Glu Ser Tyr Gly Asn Xaa Xaa Asp Ile Glu Met Ala Trp Ala Met Arg Ala Met Gln His Ala Glu 10 Val Tyr Tyr Lys Leu Ile Ser Ser Val Asp Pro Gln Phe Leu Lys Leu Thr Lys Val Asp Asp Gln Ile Tyr Ser Glu Phe Arg Lys Asn Phe Glu 40 45 Thr Leu Arg Ile Asp Val Leu Xaa Pro Glu Xaa Leu Lys Ser Glu Ser 60 Ala Lys Glu Pro Pro Gly Tyr Asn Ser Leu Pro Leu Lys Leu Leu Gly 75 Thr Gly Lys Ala Ile Thr Lys Leu Phe Ile Ser Val Phe Arg Thr Lys 90 Lys Glu Arg Lys Glu Ser Thr Met Glu Glu Lys Lys Glu Leu Thr Val

```
105
                                        110
    100
 Glu Lys Lys Arg Thr Pro Arg Met Glu Glu Arg Lys Glu Leu Ile Val
                                    125 130
         120
 Glu Lys Lys Lys Arg Lys Glu Ser Thr Glu Lys Thr Lys Leu Thr Lys
               135
                                 140
 Glu Glu Lys Lys Gly Lys Lys Leu Thr Lys Lys Ser Thr Lys Val Val
                                                160
            150
                              155
 Lys Lys Leu Cys Lys Val Tyr Arg Glu Gln His Ser Arg Ser Tyr Asp
                          170
                                            175
 Ser Ile Glu Thr Thr Ser Thr Thr Val Leu Leu Ala Gln Thr Pro Leu
   180 "
                      185
 Val Lys Cys Lys Phe Leu Tyr Asn
        ₃ 200
12.00
```

<210> 464
<211> 61
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1

<400> 464

 Met
 Thr
 Phe
 Arg
 His
 Gln
 Asp
 Asn
 Ser
 Leu
 Met
 Phe
 Phe
 Met
 Met
 Met

 Ala
 Thr
 Cys
 Thr
 Ser
 Asn
 Val
 Gly
 Phe
 Thr
 His
 Thr
 Thr
 Met
 Asn
 Cys

 -5
 1
 5
 5
 10
 10

 Ser
 Leu
 Thr
 Ser
 Phe
 Leu
 Leu
 Arg
 Val
 Leu
 Leu

 10
 20
 20
 25
 25
 25

 11e
 Lys
 Phe
 Gly
 Tyr
 Asp
 Arg
 Lys
 Ser
 Thr
 Ile
 Lys
 Ser

 30
 30
 35
 35
 40
 40
 40

<210> 466 <211> 215 <212> PRT <213> Homo sapiens

<220>

```
<221> SIGNAL "
 <222> -54..-1
 <400> 466
Met Asn Xaa Tyr Ala Ser Pro Phe Asn Xaa Gln Leu Xaa Tyr Leu Xaa
                 -50
Leu Ser Arg Phe Glu Cys Val His Arg Asp Gly Arg Val Ile Thr Leu
                                 -30
                                                     -25
 Ser Tyr Gln Glu Gln Glu Leu Gln Asp Phe Leu Leu Ser Gln Met Ser
         -20
                            -15
Gln His Gln Val His Ala Val Gln Gln Leu Ala Lys Val Met Gly Trp
. Gln Val Leu Ser Phe Ser Asn His Val Gly Leu Gly Pro Ile Glu Ser
                                   20
Xaa Gly Asn Ala Ser Ala Ile Thr Val Ala Pro Gln Val Val Thr Met
            30
                                 35
Leu Phe Gln Phe Val Met Asp Leu Lys Val Ala Ala Arg Leu Trp Phe
 Ser Phe Leu Val Thr Asn Val Lys Thr Phe Gln Lys Val Met Phe Tyr
                       65
                                           70
Lys Ile Thr Asn Gly Val Ile Phe Val Gly His Ser Lys Lys Phe Ser
                    80
                                        85
Gly Ile Lys Trp Lys Val Xaa Ile Leu Phe Ile Lys Trp Xaa Cys Leu
                95
                                    100
Cys Leu His Leu Ala Leu Val Tyr Tyr Asp Phe Phe Gln Met Phe Pro
                                115
Lys Xaa Val Ser Xaa Asn Phe Asp Leu Lys Cys Leu Gln Ile Asn Tyr
                            130
Lys His Lys Glu Glu Ile Thr Ser Lys Arg Val Leu Phe Leu Lys Ile
                        145
Ile Ile Arg Lys Cys Phe Ile
```

```
<210> 468
<211> 85
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1
```

<400> 468

Met Cys Ser His Ala Ser Met Ser Phe His Thr Leu Phe His Leu Leu -10 -15 -20 Phe Leu Pro His Tyr Ile Glu Thr Phe Lys Pro Gln Ser Lys His Cys 1 Phe Phe Trp Ile Ala Ala Phe Leu Thr Ser Leu Leu Thr Pro Gln Ser 20 .15 Leu Gln Gly Phe His Ser Ser Leu Cys Ala Leu Arg Ser Gln His Phe 35 30 Pro Ser Thr Cys Asn Cys Phe Cys Tyr Leu Thr Ile Ile Ala Leu Xaa 50 45 Tyr Trp Asp Asn Leu 60

1 5 10 15
Cys Leu Pro Cys Leu Ser Trp Asn Lys Lys Gly Asn Val Leu Gln Leu 20 25 30
Pro Asn Phe 35

<210> 470 <211> 67 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -43..-1

<210> 471 <211> 63 <212> PRT <213> Homo sapiens <210> 472

```
<220>
<221> SIGNAL
<222> -15..-1
<400> 471
Met Gly Ile Leu Ser Thr Val Thr Ala Leu Thr Phe Ala Arg Ala Leu
                   -10
                                       -5
Asp Gly Cys Arg Asn Gly Ile Ala His Pro Ala Ser Glu Lys His Arg
           5 "
                               10.
Leu Glu Lys Cys Arg Glu Leu Glu Ser Ser His Ser Ala Pro Gly Ser
       20
                           25
                                 ...
Thr Gln His Arg Arg Lys Thr Thr Arg Arg Asn Tyr Ser Ser Ala
           40
                                          45
```

```
<211> 179
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -58..-1 ...
<400> 472
Met Ser Thr Gly Gln Leu Tyr Arg Met Glu Asp Ile Gly Arg Phe His
           -55
                  · -50
Ser Gln Gln Pro Gly Ser Leu Thr Pro Ser Ser Pro Thr Val Gly Glu
                           -35
                                               -30
Ile Ile Tyr Asn Asn Thr Arg Asn Thr Leu Gly Trp Ile Gly Gly Ile
                       -20
                                           -15
Leu Met Gly Ser Phe Gln Gly Thr Ile Ala Gly Gln Gly Thr Gly Ala
           -5
Thr Ser Ile Ser Glu Leu Cys Lys Gly Gln Glu Leu Glu Pro Ser Gly
           10
                               15
Ala Gly Leu Thr Val Ala Pro Pro Gln Ala Val Ser Leu Gln Gly Ile
                           30
Tyr Thr Leu Pro Trp Leu Leu Gln Leu Phe His Ser Thr Ala Leu Xaa
                       45
Xaa Xaa Gln Gln Pro Asn Gly Ser Leu Ser Leu Asn Ile Ser Ser Ser
                   60
His Ala Pro Xaa Pro Xaa Thr Cys Thr Leu Glu Pro Gly Val Asp Pro
               75
                                   80
Thr Arg Xaa Val Cys Ile Asn Pro His Pro Pro Pro Pro Ile Leu Lys
                               95
Xaa Pro Leu Ser Pro Tyr Pro Lys Pro Gln Leu Gly Thr His Ala Gly
                           110
Gln Val Asn
   120
```

```
<210> 473
<211> 238
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -71..-1
```

<400> 473 Met Xaa Xaa Phe Thr Asp Pro Ser Ser Val Asn Glu Lys Lys Arg Arg -65 Glu Arg Glu Glu Arg Gln Asn Ile Val Leu Trp Arg Gln Pro Leu Ile -45 -50 Thr Leu Gln Tyr Phe Ser Leu Glu Ile Leu Val Ile Leu Lys Glu Trp -35 -30 Thr Ser Lys Leu Trp His Arg Gln Ser Ile Val Val Ser Phe Leu Leu -15 Leu Leu Ala Gly Leu Ile Ala Thr Tyr Tyr Val Glu Gly Val His Gln Gln Tyr Val Gln Arg Ile Glu Lys Gln Phe Leu Leu Tyr Ala Tyr Trp 15 Ile Gly Leu Gly Ile Leu Ser Ser Val Gly Leu Gly Thr Gly Leu His 30 Thr Phe Leu Leu Tyr Leu Gly Pro His Ile Ala Ser Val Thr Leu Ala 50 Ala Tyr Glu Cys Asn Ser Val Asn Phe Pro Glu Pro Pro Tyr Pro Asp 65 Gln Ile Ile Cys Pro Asp Glu Glu Gly Thr Glu Gly Thr Ile Ser Leu 80 Trp Ser Ile Ile Ser Lys Val Arg Ile Glu Ala Cys Met Trp Gly Ile 100 95 Gly Thr Ala Ile Gly Glu Leu Pro Pro Tyr Phe Met Ala Arg Ala Ala 115 110 Arg Leu Ser Gly Ala Glu Pro Asp Asp Glu Glu Tyr Gln Glu Phe Glu 130 125 Glu Met Leu Glu His Ala Glu Ser Ala Gln Val Arg Thr Val Gly Ile 145 Glu Asn Arg Thr Leu Tyr Phe Phe Leu Lys Arg Leu Leu Arg 160

<210> 474 <211> 178 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<222> -37..-1 <400> 474

Met Glu Arg Gln Ser Arg Val Met Ser Glu Lys Asp Glu Tyr Gln Phe -35 -30 Gln His Gln Gly Ala Val Glu Leu Leu Val Phe Asn Phe Leu Leu Ile -15 -10 Leu Thr Ile Leu Thr Ile Trp Leu Phe Lys Asn His Arg Phe Arg Phe Leu His Glu Thr Gly Gly Ala Met Val Tyr Gly Leu Xaa Met Gly Leu 20 Ile Leu Xaa Tyr Ala Thr Ala Pro Thr Asp Ile Glu Ser Gly Xaa Val 35 Tyr Asp Cys Val Lys Leu Thr Phe Ser Pro Ser Thr Leu Leu Val Asn 50 Ile Thr Asp Gln Val Tyr Glu Tyr Lys Tyr Lys Arg Glu Ile Ser Gln 70 65 His Xaa Ile Asn Pro His Xaa Gly Asn Ala Ile Leu Glu Lys Met Thr 85 Phe Asp Pro Xaa Ile Phe Phe Asn Val Leu Leu Pro Pro Ile Ile Phe

```
His Ala Gly Tyr Ser Leu Lys Lys Arg His Phe Phe Gln Asn Leu Gly
110 115 120

Ser Ile Leu Thr Tyr Ala Phe Leu Gly Thr Ala Ile Ser Cys Ile Val
125 130 135

Ile Gly
140
```

<210> 475 <211> 96 <212> PRT <213> Homo sapiens

<221> SIGNAL <222> -21..-1

70

65 .

<210> 476 <211> 41 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -24..-1

<210> 477
<211> 113
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27..-1

<210> 478
<211> 250
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1

<400> 478 Met Arg Ile Leu Gln Leu Ile Leu Leu Ala Leu Ala Thr Gly Leu Val -10 -15 Gly Gly Glu Thr Arg Ile Ile Lys Gly Phe Glu Cys Lys Pro His Ser Gln Pro Trp Gln Ala Ala Leu Phe Glu Lys Thr Arg Leu Leu Cys Gly 25 Ala Thr Leu Ile Ala Pro Arg Trp Leu Leu Thr Ala Ala His Cys Leu 40 Lys Pro Arg Tyr Ile Xaa His Leu Gly Gln His Asn Leu Gln Lys Glu 55 Glu Gly Cys Glu Gln Thr Arg Thr Ala Thr Glu Ser Phe Pro His Pro 70 Gly Phe Asn Asn Ser Leu Pro Asn Lys Asp Xaa Xaa Asn Asp Ile Met 85 Leu Val Xaa Met Xaa Ser Pro Val Ser Ile Thr Trp Ala Val Arg Pro 100 105 Leu Thr Leu Ser Ser Arg Cys Val Thr Ala Gly Thr Ser Cys Leu Ile 120 115 Ser Gly Trp Gly Ser Thr Ser Ser Pro Gln Leu Arg Leu Pro His Thr 135 130 Leu Arg Cys Ala Asn Ile Thr Ile Ile Glu His Gln Lys Cys Glu Asn 150 Ala Tyr Pro Gly Asn Ile Thr Asp Thr Met Val Cys Ala Ser Val Gln 170 165 Glu Gly Gly Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val 180 185 Cys Asn Gln Ser Leu Gln Gly Ile Ile Ser Trp Gly Gln Asp Pro Cys 200 Ala Ile Thr Arg Lys Pro Gly Val Tyr Thr Lys Val Cys Lys Tyr Val 215 210

Asp Trp Ile Gln Glu Thr Met Lys Asn Asn

```
<210> 479
<211> 151
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 479
Met Ala Ala Ser Thr Ser Met Val Pro Val Ala Val Thr Ala Ala Val
                        -15
                                            -10
Ala Pro Val Leu Ser Ile Asn Ser Asp Phe Ser Asp Leu Arg Glu Ile
Lys Lys Gln Leu Leu Leu Ile Ala Gly Leu Thr Arg Glu Arg Gly Leu
                                20
Leu His Ser Ser Lys Trp Ser Ala Glu Leu Ala Phe Ser Leu Pro Ala
                            35
Leu Pro Leu Ala Glu Leu Gln Pro Pro Pro Pro Ile Thr Glu Glu Asp
                        50
Ala Gln Asp Met Asp Ala Tyr Thr Leu Ala Lys Ala Tyr Phe Asp Val
                   65
                                        70
Lys Glu Tyr Asp Arg Ala Ala His Phe Leu His Gly Cys Asn Ala Arg
                80
                                    85
Lys Ala Tyr Phe Leu Tyr Met Tyr Ser Arg Tyr Leu Val Arg Ala Ile
            95 ' '
                             100
Leu Lys Cys His Ser Ala Phe Ser Glu Thr Ser Ile Phe Arg Thr Asn
       110
Gly Lys Val Lys Ser Phe Lys
    125
<210> 480
<211> 239
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 480
Met Pro Arg Lys Arg Lys Cys Asp Leu Arg Ala Val Arg Val Gly Leu
                    -20
Leu Leu Gly Gly Gly Val Tyr Gly Ser Arg Phe Arg Phe Thr Phe
Pro Gly Cys Arg Ala Leu Ser Pro Trp Arg Val Arg Xaa Gln Arg Arg
                            15
Arg Cys Glu Met Ser Thr Met Phe Ala Asp Thr Leu Leu Ile Val Phe
                        30
Ile Ser Val Cys Thr Ala Leu Leu Ala Glu Gly Ile Thr Trp Val Leu
                    45
Val Tyr Arg Thr Asp Lys Tyr Lys Arg Leu Lys Ala Glu Val Glu Lys
```

Gln Ser Lys Lys Leu Glu Lys Lys Lys Glu Thr Ile Thr Glu Ser Ala

Gly Arg Gln Lys Lys Lys Ile Glu Arg Xaa Xaa Xaa Xaa Leu Xaa

Asn Asn Asn Arg Asp Leu Ser Met Val Arg Met Lys Ser Met Phe Ala 110 Ile Gly Phe Cys Phe Thr Ala Leu Met Gly Met Phe Asn Ser Ile Phe 125 130 Asp Gly Arg Val Val Ala Lys Leu Pro Phe Thr Pro Leu Ser Xaa Xaa 145 Xaa Gly Leu Ser His Arg Asn Leu Leu Gly Asp Asp Thr Thr Asp Cys 160 Ser Phe Ile Phe Leu Xaa Ile Leu Cys Thr Met Ser Ile Arg Gln Asn 175 170 .180 Ile Gln Lys 'Ile Leu Gly Leu Ala Pro Ser Arg Ala Ala Thr Lys Gln 190 195 Ala Gly Gly Phe Leu Gly Pro Pro Pro Pro Ser Gly Lys Phe Ser 205

<210> 481 <211> 208 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -92..-1

<400> 481

Met Arg Glu Pro Gln Lys Arg Thr Ala Thr Ile Ala Lys Xaa Xaa Ala -90 , , -85 Xaa Glu Gly Leu Arg Asp Pro Tyr Gly Arg Leu Cys Gly Ser Glu His -70 -65 Pro Arg Arg Pro Pro Glu Arg Pro Glu Glu Asp Pro Ser Thr Pro Glu -50 -55 Glu Ala Ser Thr Thr Pro Glu Glu Ala Ser Ser Thr Ala Gln Ala Gln -35 Lys Pro Ser Val Pro Arg Ser Asn Phe Gln Gly Thr Lys Lys Ser Leu -20 Leu Met Ser Ile Leu Ala Leu Ile Phe Ile Met Gly Asn Ser Ala Lys -5 Glu Ala Leu Val Trp Lys Val Leu Gly Lys Leu Gly Met Gln Pro Gly 10 Arg Xaa His Ser Ile Phe Gly Asp Pro Lys Lys Ile Val Thr Glu Xaa 25 30 Phe Val Arg Arg Gly Tyr Leu Ile Tyr Xaa Pro Val Pro Arg Xaa Ser 40 45 Pro Val Glu Tyr Xaa Phe Phe Trp Gly Pro Arg Ala His Val Glu Ser 60 Ser Xaa Leu Lys Xaa Xaa His Phe Val Ala Arg Val Arg Asn Arg Cys Ser Lys Asp Trp Pro Cys Asn Tyr Asp Trp Asp Ser Asp Asp Asp Ala 95 Glu Val Glu Ala Ile Leu Asn Ser Gly Ala Xaa Gly Tyr Ser Ala Pro 105 110

<210> 482 <211> 86 <212> PRT <213> Homo sapiens

```
<221> SIGNAL **
<222> -39..-1 *
```

<400> 482

Met Asn Val Gly Thr Ala His Xaa Xaa Val Asn Pro Asn Thr Arg Val

Met Asn Ser Arg Gly Ile Trp Leu Ser Tyr Val Leu Ala Ile Gly Leu
-20 -15 -10

Leu His Ile Val Leu Leu Ser Ile Pro Phe Val Ser Val Pro Val Val -5 5

Trp Thr Leu Thr Asn Leu Ile His Asn Met Gly Met Tyr Ile Phe Leu 10 20 25

His Thr Val Lys Gly Thr Pro Phe Glu Thr Pro Asp Gln Gly Lys Ala  $30 \hspace{1.5cm} 35 \hspace{1.5cm} 40$ 

Arg Leu Leu Thr His Trp 45

<210> 483

<211> 40

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -27..-1

<400> 483

Met Arg Thr Leu Phe Gly Ala Val Arg Ala Pro Phe Ser Ser Leu Thr
-25
-20
-15

Leu Leu Leu Ile Thr Pro Ser Pro Ser Pro Leu Leu Phe Asp Arg Gly
-10 -5 1 5

Leu Ser Leu Arg Ser Ala Met Ser

10

<210> 484

<211> 65

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -16..-1

<400> 484

Met Leu Gly Phe Phe Leu Phe Leu Ser Phe Val Leu Met Tyr Asp Gly
-15 -10 -5

Leu Arg Leu Phe Gly Ile Leu Ser Thr Cys Arg Val His His Thr Met

1 10 15

Asn Gln Phe Leu Ile Asp Ile Ser Ser Phe Thr Ser Arg Val Lys Lys 20 25 30

Lys Ile Phe Leu Phe Tyr Ala Phe Xaa Gly Cys Xaa Phe Gln Ser Ala 35 40 45

Thr

```
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -55..-1
<400> 485
Met Ala Met Trp Asn Arg Pro Xaa Xaa Xaa Leu Pro Gln Gln Pro Leu
                                        -45
                    -50
Xaa Ala Glu Pro Thr Ala Glu Gly Glu Pro His Leu Pro Thr Gly Arg
                                                        -25
                                    -30
Xaa Xaa Thr Glu Ala Asn Arg Phe Ala Tyr Ala Ala Leu Cys Gly Ile
                                -15
            -20
Ser Leu Ser Gln Leu Phe Pro Glu Pro Glu His Ser Ser Phe Cys Thr
                            1
Glu Phe Met Ala Gly Leu Val Xaa Trp Leu Glu Leu Ser Glu Ala Val
                    15
Leu Pro Thr Met Thr Ala Phe Ala Ser Gly Leu Gly Gly Glu Gly Xaa
                                    35
Xaa Cys Val Cys Ser Asn Phe Thr Glu Gly Pro His Leu Glu Gly Arg
                                50
Pro Asp Gly Asp His Ser Gly Pro Ser Glu Leu Leu Thr Gln Gly Trp
Ala Leu
    75
<210> 486
<211> 209
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -84..-1
<400> 486
Met Val Asn Phe Pro Gln Lys Ile Ala Gly Glu Leu Tyr Gly Pro Leu
                -80
                                     -75
Met Leu Val Phe Thr Leu Val Ala Ile Leu Leu His Gly Met Lys Thr
                                 -60
Ser Asp Thr Ile Ile Arg Glu Gly Thr Leu Met Gly Thr Ala Ile Gly
                             -45
Thr Cys Phe Gly Tyr Trp Leu Gly Val Ser Ser Phe Ile Tyr Phe Leu
                         -30
                                             -25
Ala Tyr Leu Cys Asn Ala Gln Ile Thr Met Leu Gln Met Leu Ala Leu
                    -15
                                         -10
Leu Gly Tyr Gly Leu Phe Gly His Cys Ile Val Leu Phe Ile Thr Tyr
Asn Ile His Leu Arg Ala Leu Phe Tyr Leu Phe Trp Leu Leu Val Gly
                             20
Gly Leu Ser Thr Leu Arg Met Val Ala Val Leu Val Ser Arg Thr Val
                         35
Gly Pro Thr Xaa Arg Xaa Leu Leu Cys Gly Thr Leu Ala Ala Leu His
                     50
Met Leu Phe Leu Leu Tyr Leu His Phe Ala Tyr His Lys Xaa Val Xaa
```

70

Gly Ile Leu Asp Thr Leu Glu Gly Pro Asn Ile Pro Pro Ile Gln Arg 80 85 90 Val Pro Arg Asp Ile Pro Ala Met Leu Pro Ala Ala Arg Leu Pro Thr

```
95
                           100
                                              105
Thr Val Leu Asn Ala Thr Ala Lys Ala Val Ala Val Thr Leu Gln Ser
                       115
                                          120
His
125
<210> 487
<211> 36
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -17..-1
<400> 487
Met Gly Trp Gln Arg Trp Trp Cys Phe His Leu Gln Ala Glu Ala Ser
       -15 -10
                                -5
Ala His Pro Pro Gln Gly Leu Gln Ala Gln Phe Ser Cys Cys Pro Trp
                  5
                                      10
Val Gly Ile Cys
<210> 488
<211> 44
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -29..-1
<400> 488
Met Met Ser Ser Glu Leu Arg Arg Asn Pro His Phe Leu Lys Ser Asn
          ·· -25
                                  -20
Leu Phe Leu Gln Leu Leu Val Ser His Glu Ile Val Cys Ala Thr Glu
          -10
                              - 5
Thr Val Thr Thr Asn Phe Leu Arg His Glu Lys Ala
                       10
<210> 489
<211> 163
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -52..-1
<400> 489
Met Glu His Tyr Arg Lys Ala Gly Ser Val Glu Leu Pro Ala Pro Ser
       -50
                           -45
Pro Met Pro Gln Leu Pro Pro Asp Thr Leu Glu Met Arg Val Arg Asp
                       -30
                                          -25
```

Gly Ser Lys Ile Arg Asn Leu Leu Gly Leu Ala Leu Gly Arg Leu Glu

Gly Gly Ser Ala Arg His Val Val Phe Ser Gly Ser Gly Arg Ala Ala

-10

-15

Gly Lys Ala Val Ser Cys Ala Glu Ile Val Lys Arg Arg Val Pro Gly
15

Leu His Gln Leu Thr Lys Leu Xaa Phe Leu Gln Thr Glu Asp Ser Trp
30

Val Pro Xaa Ser Pro Asp Thr Gly Leu Xaa Pro Leu Thr Val Arg Arg
45

His Val Pro Ala Xaa Trp Val Leu Leu Xaa Arg Asp Pro Leu Asp Pro
65

Asn Glu Cys Gly Tyr Gln Pro Pro Gly Ala Pro Pro Gly Leu Gly Ser
80

Met Pro Ser Ser Ser Cys Gly Pro Arg Ser Xaa Lys Arg Ala Xaa Xaa
95

Thr Arg Ser
110

<210> 490 <211> 64 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -47..-1

<210> 491 <211> 218 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -50..-1 <400> 491 Met His His Gly Leu

 Met His His Gly
 Leu
 Thr
 Pro
 Leu
 Leu
 Leu
 Gly
 Val
 His
 Glu
 Gln
 Lys
 Lys
 Leu
 Gly
 Val
 His
 Glu
 Gln
 Lys
 Lys
 Lys
 Lys
 Lys
 Lan
 Asn
 Leu
 Asn
 Ala
 Cys
 Cys
 Gly

 Ser
 Ala
 Ser
 Ile
 Val
 Ser
 Leu
 Leu
 Leu
 Glu
 Gln
 Asn
 Ile
 Asp
 Val
 Ser
 Ser
 Ser
 Ile
 Leu
 Leu
 Leu
 Glu
 Asn
 Ile
 Asp
 Val
 Ser
 Ser
 Ser
 Ile
 Asn
 Ile
 Asn
 Ile
 Asn
 Ala
 Asn
 Ile
 Asn

50 Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Lys Gly Ser Glu Asn Ser 70 Gln Pro Glu Glu Met Ser Gln Glu Pro Glu Ile Asn Xaa Gly Gly Asp 85 Arg Lys Val Glu Xaa Xaa Met Lys Lys His Gly Ser Xaa His Met Gly 100 105 Phe Pro Xaa Asn Leu Xaa Asn Gly Ala Thr Ala Asp Asn Gly Asp Asp 115 120 Gly Leu Ile Pro Pro Xaa Lys Xaa Xaa Thr Pro Glu Ser Xaa Gln Phe .. 130 135 Pro Asp Thr Glu Asn Glu Gln Tyr His Arg Asp Phe Ser Gly His Pro 150 Xaa Phe Pro Thr Thr Leu Pro Ile Lys Gln 165

<210> 492 <211> 216 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

## <400> 492

Met Val Cys Val Leu Val Leu Ala Ala Ala Gly Ala Val Ala Val -10 Phe Leu Ile Leu Arg Ile Trp Val Val Leu Arg Ser Met Asp Val Thr Pro Arg Glu Ser Leu Ser Ile Leu Val Val Ala Gly Ser Gly Gly His Thr Thr Glu Ile Leu Arg Leu Leu Gly Ser Leu Ser Asn Ala Tyr Ser Pro Arg His Tyr Val Ile Ala Asp Thr Asp Glu Met Ser Ala Asn Lys 60 55 Ile Asn Ser Phe Glu Leu Xaa Arg Xaa Asp Arg Xaa Pro Ser Asn Met 70 75 Xaa Thr Lys Tyr Tyr Ile His Arg Ile Pro Xaa Ser Arg Glu Val Gln 90 Gln Ser Trp Pro Ser Thr Val Xaa Thr Thr Leu His Ser Met Trp Leu 105 Ser Xaa Pro Leu Ile His Arg Val Lys Pro Xaa Leu Val Leu Cys Asn 120 125 Gly Pro Gly Thr Cys Val Pro Ile Cys Val Ser Ala Leu Leu Gly 135 140 Ile Leu Gly Ile Lys Lys Val Ile Ile Val Tyr Val Glu Ser Ile Cys 150 155 Arg Val Lys Thr Leu Ser Met Ser Gly Lys Ile Leu Phe His Leu Ser 170 Asn Tyr Phe Ile Val Gln Trp Pro Ala Leu Lys Glu Lys Tyr Pro Lys 185 Ser Val Tyr Leu Gly Arg Ile Val 195

<210> 493

<211> 134

<212> PRT

. ii

<220>

<221> SIGNAL <222> -29..-1

```
<213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -19..-1
 <400> 493
 Met Pro Leu Gly Ala Arg Ile Leu Phe His Gly Val Phe Tyr Ala Gly
                  -15
                                      -10
 Gly Phe Ala Ile Val Tyr Tyr Leu Ile Gln Lys Phe His Ser Arg Thr
 Leu Tyr Tyr Lys Leu Ala Val Glu Gln Leu Gln Xaa His Pro Glu Ala
                         20
''Gln Glu Ala Leu Gly Pro Pro Leu Asn Ile His Tyr Leu Lys Leu Ile
                     35
                                         40
 Asp Arg Glu Asn Phe Val Asp Ile Val Xaa Ala Lys Leu Lys Ile Pro
                 50
                                      55
 Val Ser Gly Ser Lys Ser Glu Gly Leu Leu Tyr Val His Ser Ser Arg
                                  70
 Gly Gly Pro Phe Gln Arg Trp His Leu Asp Glu Val Phe Leu Glu Leu
                             85
 Lys Asp Gly Gln Gln Ile Pro Val Phe Lys Leu Ser Gly Glu Asn Gly
 Asp Glu Val Lys Lys Glu
 <210> 494
 <211> 85
  <212> PRT
  <213> Homo sapiens
  <220>
  <221> SIGNAL
  <222> -16..-1
  <400> 494
 Met Ala Val Thr Ala Leu Ala Ala Xaa Thr Trp Leu Gly Val Trp Gly
                          -10
 Val Arg Thr Met Gln Ala Arg Gly Phe Gly Ser Asp Gln Ser Glu Asn
                                      10
  Val Asp Arg Gly Ala Gly Ser Ile Arg Glu Ala Gly Gly Ala Phe Gly
  Lys Arg Glu Gln Ala Glu Glu Glu Arg Tyr Phe Arg Ala Gln Ser Thr
                              40
  Glu Gln Leu Ala Xaa Leu Lys Lys Xaa His Glu Glu Glu Ile Val His
                          55
  His Arg Glu Gly Asp
  <210> 495
  <211> 292
  <212> PRT
  <213> Homo sapiens
```

```
<400> 495
Met His Gly Leu Leu His Tyr Leu Phe His Thr Arg Asn His Thr Phe
                                  -20
               -25
Ile Val Leu His Leu Val Leu Gln Gly Met Val Tyr Thr Glu Tyr Thr
Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu Ser Leu His Tyr
                       10
                                           15
Leu Leu Leu Pro Tyr Leu Leu Gly Val Asn Leu Phe Phe Thr
            ' , 25
                                     , 30
Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys Ala Asn Glu Leu
Leu Phe Leu His Val Tyr Glu Phe Asp Glu Xaa Met Phe Pro Lys Asn
                               60
Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala Arg Ser Xaa His
Cys Xaa Val Cys Asn Trp Cys Val His Arg Phe Xaa His His Cys Val
                       90
Trp Val Asn Asn Cys Ile Gly Ala Trp Asn Ile Arg Xaa Phe Leu Ile
                   105
                                       110
Tyr Val Leu Thr Leu Thr Ala Ser Ala Ala Thr Val Ala Ile Val Ser
               120
                                   125
Thr Thr Phe Leu Val His Leu Val Val Met Ser Asp Leu Tyr Gln Glu
                               140
Thr Tyr Ile Asp Asp Leu Gly His Leu His Val Met Asp Thr Val Phe
                           155
                                               160
Leu Ile Gln Tyr Leu Phe Leu Thr Phe Pro Arg Ile Val Phe Met Leu
                       170
                                           175
Gly Phe Val Val Leu Xaa Phe Leu Leu Gly Gly Tyr Leu Leu Phe
        1 185
                                       190
Val Leu Tyr Leu Ala Ala Thr Asn Gln Thr Thr Asn Glu Trp Tyr Arg
                                   205
              200
Xaa Asp Trp Ala Trp Cys Gln Arg Cys Pro Leu Val Ala Trp Pro Pro
                                                   225
           215
                               220
Ser Ala Glu Pro Gln Val His Arg Asn Ile His Ser His Gly Leu Arg
                          235
Xaa Asn Leu Gln Glu Ile Phe Leu Pro Ala Phe Pro Cys His Glu Arg
                       250
Lys Lys Gln Glu
260
```

```
<210> 496
<211> 122
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -56..-1
```

<400> 496

Met Thr Gly Phe Leu Leu Pro Pro Ala Ser Arg Gly Thr Arg Arg Ser -50 Cys Ser Arg Ser Arg Lys Arg Gln Thr Arg Arg Arg Asn Pro Ser -35 -30 Ser Phe Val Ala Ser Cys Pro Thr Leu Leu Pro Phe Ala Cys Val Pro -20 -15 Gly Ala Ser Pro Thr Thr Leu Ala Phe Pro Pro Val Xaa Leu Thr Gly Pro Xaa Thr Asp Gly Ile Pro Phe Ala Leu Xaa Ser Ala Ala Gly Pro Phe Cys Ala Ser Phe Pro Ser Gly Xaa Leu Ser Pro Pro Gly Pro Leu 30 35 Pro Gly Val Arg Gly Leu Pro Leu Pro Ser Val Phe Tyr Ser Cys Gly 45 50 Ala His Pro Lys Val Leu Lys Val Ala Leu

<210> 497 <211> 59 <212> PRT <213> Homo sapiens ·<220> <221> SIGNAL <222> -28..-1

<400> 497

Met Leu Xaa Leu Ser Arg Ala Thr Lys Xaa Gly Arg Ala Arg Trp Leu -20 Met Pro Val Ile Pro Ala Leu Gln Glu Ala Xaa Ala Gly Gly Ser Arg -10 -5 Gly Gln Glu Phe Glu Thr Ser Leu Ala Asn Met Glu Thr Glu Ala Gly 10 20 Glu Leu Leu Lys Pro Arg Arg Arg Leu Gln 25

<210> 498 <211> 99 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -13..-1

<400> 498

Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg Arg Pro -10 Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu Ala His 10 Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys Trp Arg Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn Ser Ser 40 45 Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr Pro Met 60 Arg Arg Ser Ser Cys His Leu Glu Cys Xaa Val Ile Phe Leu Leu Gly 70 75 Arg Gln Leu 85

<210> 499 <211> 99 <212> PRT <213> Homo sapiens

<222> -15..-1

```
<220>
<221> SIGNAL
<222> -13..-1
<400> 499
Met His Leu Leu Ser Asn Trp Ala Asn Pro Ala Ser Ser Arg Arg Pro
                                -5
Ser Met Ala Ala Ser Gly Thr Ser Trp Ile Ser Ser Thr Leu Ala His
Ser Leu Ser Leu Arg Asp Val Ser Glu Arg Leu Cys Ser Cys Trp Arg
Thr Ile Ser Met Gly Pro Cys Ala Arg Gly Ser Pro Met Asn Ser Ser
Gly Val His Arg Lys Ser Ser Arg Leu Phe Tyr Ile Arg Thr Pro Met
Arg Arg Ser Ser Cys His Leu Xaa Cys Gln Val Ile Phe Leu Leu Gly
Arg Gln Leu
    85
<210> 500
<211> 108
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 500
Met Ser Leu Thr Ser Ser Ser Ser Val Arg Val Glu Trp Ile Ala Ala
                    -20
Val Thr Ile Ala Ala Gly Thr Ala Ala Ile Gly Tyr Leu Ala Tyr Lys
Arg Phe Tyr Val Lys Asp His Arg Asn Lys Ala Met Ile Asn Leu His
       10 ..
Ile Gln Lys Asp Asn Pro Lys Ile Val His Ala Phe Asp Met Glu Asp
Leu Gly Asp Lys Ala Val Tyr Cys Arg Cys Trp Arg Ser Lys Lys Phe
                                        50
Pro Phe Cys Asp Gly Ala His Thr Lys His Asn Glu Glu Thr Gly Asp
Asn Val Gly Pro Leu Ile Ile Lys Lys Glu Thr
<210> 501
<211> 183
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
```

```
Gln Gly Arg Arg Leu Gly Ala Glu Ser Arg Thr Leu Leu Val Ile Ala
                            25
His Pro Asp Asp Glu Ala Met Phe Phe Ala Pro Thr Val Leu Gly Leu
                        40
                                            45
Ala Arg Leu Arg His Trp Val Tyr Leu Leu Cys Phe Ser Ala Gly Asn
                    55
                                       60
Tyr Tyr Asn Gln Gly Glu Thr Arg Lys Lys Glu Leu Leu Gln Ser Cys
                70
                                   75
Asp Val Leu Gly Ile Pro Leu Ser Ser Val Met Ile Ile Asp Asn Arg
           85
                                90
Asp Phe Pro Xaa Asp Pro Gly Met Gln Trp Asp Thr Xaa His Val Ala
        100 .
                            105
Xaa Val Leu Leu Gln His Ile Glu Val Asn Gly Ile Asn Leu Val Val
                        120
                                            125
Thr Phe Asp Ala Gly Gly Xaa Ser Gly His Ser Asn His Ile Ala Leu
                    135
                                       140
Tyr Ala Ala Val Arg Lys Leu Glu Gly Gln Ile Cys Lys Pro Cys Gly
               150
Thr Gly Gln Asp Phe Lys Glu
            165
```

<210> 502 <211> 98 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -15..-1

<400> 502

 Met
 Glu
 Ala
 Met
 Trp
 Leu
 Leu
 Cys
 Val
 Ala
 Leu
 Ala
 Val
 Leu
 Ala
 Trp
 Trp
 Leu
 Trp
 Ala
 Ser
 Ser
 Glu
 Arg
 Met
 Lys
 Ser
 Arg
 Glu
 Arg
 Glu
 Arg
 Met
 Leu
 Leu
 Leu
 Arg
 Glu
 Ala
 Glu
 Ser
 Arg
 Thr
 Leu
 Leu
 Val
 Ile
 Ala
 Ala
 Arg
 Arg
 Arg
 Ala
 Ala
 Glu
 Ser
 Arg
 Arg</th

<210> 503 <211> 183 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -57..-1

<400> 503
Met Asp Val Thr Gly Asp Glu Glu Glu Glu Ile Lys Gln Glu Ile Asn
-55
-50
-45

```
Met Leu Lys Lys Tyr Ser His His Arg Asn Ile Ala Thr Tyr Tyr Gly
                       -35
Ala Phe Ile Lys Lys Asn Pro Pro Gly Met Asp Asp Gln Leu Trp Leu
                   -20
                                       -15
Val Met Glu Phe Cys Gly Ala Gly Ser Val Thr Asp Leu Ile Lys Asn
Thr Lys Gly Asn Thr Leu Lys Glu Glu Trp Ile Ala Tyr Ile Cys Xaa
                           15
Glu Ile Leu Arg Gly Leu Xaa His Leu His Gln His Lys Val Ile His
                        30
                                           35
Arg Xaa Ile Lys Gly Gln Asn Val Leu Leu Thr Glu Asn Ala Glu Val
Lys Leu Val Asp Phe Gly Xaa Xaa Ala Gln Leu Asp Arg Thr Val Gly
                60 .
                                . 65
Arg Xaa Asn Thr Phe Ile Gly Thr Pro Tyr Trp Met Ala Pro Xaa Val
Ile Ala Cys Asp Glu Asn Pro Xaa Ala Thr Tyr Asp Phe Lys Xaa Asp
                           95
Leu Trp Ser Leu Gly Ile Thr Ala Ile Glu Met Ala Glu Gly Leu Pro
                   110
                                           115
Leu Ser Val Thr Cys Thr Pro
```

<210> 504

<211> 140

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -14..-1

<400> 504

Met Phe Leu Thr Ala Leu Leu Trp Arg Gly Arg Ile Pro Gly Arg Gln
-10 -5 1

Trp Ile Gly Lys His Arg Arg Pro Arg Phe Val Ser Leu Arg Ala Lys
5 10 15

Gln Asn Met Ile Arg Arg Leu Glu Ile Glu Ala Glu Asn His Tyr Trp 20 25 30

Leu Ser Met Pro Tyr Met Thr Arg Glu Gln Glu Arg Gly His Ala Ala
35 40 45 50

Leu Arg Arg Glu Ala Phe Glu Ala Ile Lys Ala Ala Ala Thr Ser
55 60 65

Lys Phe Pro Pro His Arg Phe Ile Ala Asp Gln Leu Asp His Leu Asn

Xaa His Gln Glu Met Val Leu Ile Leu Ser Arg His Pro Trp Ile Leu
85 90 95

Trp Ile Thr Glu Leu Thr Ile Phe Thr Trp Ser Gly Leu Lys Asn Cys 100 105 110

Ser Leu Cys Glu Asn Glu Leu Trp Thr Ser Leu Tyr 115 120 125

<210> 505

<211> 59

<212> PRT

<213> Homo sapiens

<221> SIGNAL <222> -14..-1

<400> 505

Met Ala Ala Leu Val Thr Val Leu Phe Thr Gly Val Arg Arg Leu His

Cys Ser Ala Xaa Leu Gly Arg Ala Ala Ser Gly Xaa Tyr Ser Arg Asn 5 10 15

Trp Leu Pro Thr Pro Pro Ala Thr Gly Pro Leu Pro Ser Ser Gln Thr 20 25 30

Gly His Met Arg Met Ala Ala Leu Leu Pro Gln 35 40 45

<210> 506

<211> 101

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -36..-1

<400> 506

Met Gly Pro Tyr Asn Val Ala Val Pro Ser Asp Val Ser His Ala Arg -35 -30 -25

Phe Tyr Phe Leu Phe His Arg Pro Leu Arg Leu Leu Asn Leu Leu Ile
-20 -15 -10 -5

Leu Ile Glu Gly Ser Val Val Phe Tyr Gln Leu Tyr Ser Leu Leu Arg 1 5 10

Ser Glu Lys Trp Asn His Thr Leu Ser Met Ala Leu Ile Leu Phe Cys 15 20 25

Asn Tyr Tyr Val Leu Phe Lys Leu Leu Arg Asp Arg Xaa Xaa Leu Gly 30 35 40

Arg Ala Tyr Ser Tyr Pro Leu Asn Ser Tyr Glu Leu Lys Ala Asn Xaa 45 50 55 60

Ala Ala Ser Xaa Gln

55

<210> 507

<211> 341

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -55..-1

<400> 507

Met Arg Lys Val Val Leu Ile Thr Gly Ala Ser Ser Gly Ile Gly Leu
-55 -50 -45 -45

Ala Leu Cys Lys Arg Leu Leu Ala Glu Asp Asp Glu Leu His Leu Cys
-35 -30 -25

Leu Ala Cys Arg Asn Met Ser Lys Ala Glu Ala Val Cys Ala Ala Leu
-20 -15 -10

Leu Ala Ser His Pro Thr Ala Glu Val Thr Ile Val Gln Val Asp Val
-5 1 5

Ser Asm Leu Gln Ser Phe Phe Arg Ala Ser Lys Glu Leu Lys Gln Arg

Phe Gln Arg Leu Asp Cys Ile Tyr Leu Asn Ala Gly Ile Met Pro Asn 35 Pro Gln Leu Asn Ile Lys Ala Leu Phe Phe Gly Leu Phe Ser Arg Lys Val Ile His Met Phe Ser Thr Ala Glu Gly Leu Leu Thr Gln Gly Asp Lys Ile Thr Ala Asp Gly Leu Gln Glu Val Phe Glu Thr Asn Val Phe 80 Gly His Phe Ile Leu Ile Arg Glu Leu Glu Pro Leu Leu Cys His Ser . . 95 100 Asp Asn Pro Ser Gln Leu Ile Trp Thr Ser Ser Arg Ser Ala Arg Lys 110 115 Ser Asn Phe Ser Leu Glu Asp Phe Gln His Ser Lys Gly Lys Glu Pro 130 Tyr Ser Ser Ser Lys Tyr Ala Thr Asp Leu Leu Ser Val Ala Leu Asn 145 Arg Asn Phe Asn Gln Gln Gly Leu Tyr Ser Asn Val Ala Cys Pro Gly 160 Thr Ala Leu Thr Asn Leu Thr Tyr Gly Ile Leu Pro Pro Phe Ile Trp 175 180 Thr Leu Leu Met Pro Ala Ile Leu Leu Leu Arg Phe Phe Ala Asn Ala 190 195 , 200 Phe Thr Leu Thr Pro Tyr Asn Gly Thr Glu Ala Leu Val Trp Leu Phe 205 210 His Gln Lys Pro Glu Ser Leu Asn Pro Leu Ile Lys Tyr Leu Ser Ala 225 Thr Thr Gly Phe Gly Arg Asn Tyr Ile Met Thr Gln Lys Met Asp Leu 240 245 Asp Glu Asp Thr Ala Glu Lys Phe Tyr Gln Lys Leu Leu Glu Leu Glu 255 260 Lys His Ile Arg Val Thr Ile Gln Lys Thr Asp Asn Gln Ala Arg Leu 275 270 Ser Gly Ser Cys Leu 285

<210> 508 <211> 108 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<400> 508

<222> -42..-1

 Met His Ile Leu Gln Leu Leu Thr Thr Val Asp Asp Gly Ile Gln Ala -40
 -40
 -35
 -35
 -30
 Ile Gln Ala -30

 Ile Val His Cys Pro Asp Thr Gly Lys Asp Ile Trp Asn Leu Leu Phe -25
 -20
 -15

 Asp Leu Val Cys His Glu Phe Cys Gln Ser Asp Asp Pro Ala Ile Ile -10
 5

 Leu Gln Xaa Gln Lys Thr Val Leu Ala Ser Val Phe Ser Val Leu Ser 10
 20

 Ala Ile Tyr Ala Ser Gln Thr Glu Gln Xaa Tyr Leu Lys Ile Xaa Lys 25
 30

 Gly Asp Gly Gly Ser Gly Ser Lys Gly Arg Pro Xaa Xaa Gln Thr Glu 40
 45

 Xaa Phe Leu Cys Ile Ser Lys Pro Ser Ser Phe Leu 55

```
<210> 509
<211> 80
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL .
<222> -26..-1
<400> 509
Met Glu Glu Ile Ser Ser Pro Leu Val Glu Phe Val Lys Val Leu Cys
                        -20
                                            -15
Thr Asn Gln Val Leu Ile Thr Ala Arg Ala Val Pro Thr Lys Lys Ala
                    - 5
Ser Val Arg Cys Val Glu Lys Arg Phe Trp Ile Pro Lys Thr Thr Ser
            10
                                15
Lys His Leu Ser Arg Cys Ile Asp Gly Ile Ser Gly Phe Leu Asn Asp
                            30
                                                35
Phe Thr Phe Cys Leu Glu Phe Ser Arg His Arg Cys Gln Leu Thr Glu
                                            50
<210> 510
<211> 158
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -44..-1
<400> 510
Met Ala Gly Phe Leu Asp Asn Phe Arg Trp Pro Glu Cys Glu Cys Ile
                                  -35
                -40
Asp Trp Ser Glu Arg Arg Asn Ala Val Ala Ser Val Val Ala Gly Ile
                                -20
Leu Phe Phe Thr Gly Trp Trp Ile Met Ile Asp Ala Ala Val Val Tyr
Pro Lys Pro Glu Gln Leu Asn His Ala Phe His Thr Cys Gly Val Phe
                    10
                                        15
Ser Thr Leu Ala Phe Phe Met Ile Asn Ala Val Ser Asn Ala Gln Val
                25
                                    30
Arg Gly Asp Ser Tyr Glu Ser Gly Cys Leu Gly Arg Thr Gly Ala Arg
                                45
Val Trp Leu Phe Ile Gly Phe Met Leu Met Phe Gly Ser Leu Ile Ala
                            60
Ser Met Trp Ile Leu Phe Gly Ala Tyr Val Thr Gln Asn Thr Asp Val
Tyr Pro Gly Leu Ala Val Phe Phe Gln Asn Ala Leu Ile Phe Phe Ser
                    90
                                        95
Thr Leu Ile Tyr Lys Phe Gly Arg Thr Glu Glu Leu Trp Thr
```

110

<210> 511 <211> 130 <212> PRT <213> Homo sapiens

```
<220>
<221> SIGNAL
<222> -28..-1
```

<400> 511 Met Asn Trp Glu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu -25 -20 -15 Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu -10 Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu 10 Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu 60 Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu . 75 Thr Asp Thr Gly Ser His Glu Ser Gly Tyr Gln Ser Cys Ser Pro Gly 95. Ile Trp

<210> 512 <211> 199 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<400> 512

<222> -62..-1

Met Ser Gln Arg Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg -55 Xaa Leu Ile Glu Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys -40 Val Leu Pro His Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val -25 -20 Asn Ser Ile Leu Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys -10 Ala Ser Lys His Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro 25 Val Gln Ser Asn Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys 40 Thr Ile Gly Asn Asn Gly Asn Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr 90 Met Pro Thr Trp Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg 105 110 Ile Glu Asn Phe Lys Ser Gly Val Asp Ala Xaa Ser Ser Tyr Phe Lys 120 125 Ile Phe Lys Thr Lys His Asp

```
<210> 513
<211> 180
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 513
Met Asn Thr Val Leu Ser Arg Ala Asn Ser Leu Phe Ala Phe Ser Leu
                                       -15
                    -20
Ser Val Met Ala Ala Leu Thr Phe Gly Cys Phe Ile Xaa Thr Ala Phe
               -5
Lys Asp Arg Ser Val Pro Val Arg Leu His Val Ser Arg Ile Met Leu
                           15
Lys Asn Val Glu Asp Phe Thr Gly Pro Arg Glu Arg Ser Asp Leu Gly
             30
Phe Ile Thr Phe Asp Ile Thr Ala Asp Leu Glu Asn Ile Phe Asp Trp
                    45
                                       50
Asn Val Lys Gln Leu Phe Leu Tyr Leu Ser Ala Glu Tyr Ser Thr Lys
                                    65
                60
Asn Asn Ala Leu Asn Gln Xaa Val Leu Trp Asp Lys Ile Val Leu Arg
                                80
Gly Asp Asn Pro Lys Leu Leu Lys Asp Met Lys Thr Lys Tyr Phe
Phe Phe Asp Asp Gly Asn Gly Leu Xaa Gly Asn Arg Asn Val Thr Leu
                        110
                                           115
Thr Leu Ser Trp Asn Val Val Pro Asn Ala Gly Ile Leu Pro Leu Val
                                       130
                   125
Thr Gly Ser Gly His Val Ser Val Pro Phe Pro Asp Thr Tyr Glu Ile
                                    145
Thr Lys Ser Tyr
            155
 <210> 514
```

<211> 120 <212> PRT <213> Bos taurus

<400> 514

 Met
 Met
 Thr
 Gly
 Arg
 Gln
 Gly
 Arg
 Ala
 Thr
 Phe
 Gln
 Phe
 Leu
 Pro
 Asp

 Glu
 Ala
 Arg
 Ser
 Leu
 Pro
 Pro
 Pro
 Lys
 Leu
 Thr
 Asp
 Pro
 Arg
 Leu
 Ala
 Ile
 Asp
 Pro
 Arg
 Ala
 Ile
 Asp
 Asp
 Asp
 Ala
 Ile
 Asp
 Asp
 Asp
 Ala
 Ile
 Asp
 Lys
 Asp
 Lys
 Thr
 Tyr
 Gly
 Gly
 Lys
 Lys
 Thr
 Tyr
 Ile
 Lys
 Asp
 Gln
 Asp

 For
 Tyr
 Asp
 Asp
 His
 Asp
 Lys
 Lys
 Thr
 Tyr
 Ile
 Lys
 Asp
 Ile
 Lys
 Asp
 Lys

44

```
<210> 515
<211> 1082
<212> DNA
<213> Homo sapiens
<400> 515
                                                                   60
gateccagae eteggettge agtagtgtta gaetgaagat aaagtaagtg etgtttggge
                                                                  120
taacaggate teetettgea gtetgeagee caggaegetg attecageag egeettaceg
cqcagcccga agattcacta tggtgaaaat cgccttcaat acccctaccg ccgtgcaaaa
                                                                  180
                                                                  240
ggaggaggcg cggcaagacg tggaggccct cctgagccgc acggtcagaa ctcagatact
                                                                  300
gaccggcaag gagctccgag ttgccaccca ggaaaaagag ggctcctctg ggagatgtat
                                                                  3,60
gettactete traggeettt catteatett ggeaggaett attgttggtg gageetgeat
                                                                  420
ttacaagtac ttcatgccca agagcaccat ttaccgtgga gagatgtgct tttttgattc
tgaggatect geaaatteee ttegtggagg agageetaae tteetgeetg tgaetgagga.
                                                                  480
ggctgacatt cgtgaggatg acaacattgc aatcattgat gtgcctgtcc ccagtttctc
                                                                  540
                                                                  600
tgatagtgac cctgcagcaa ttattcatga ctttgaaaag ggaatgactg cttacctgga
cttgttgctg gggaactgct atctgatgcc cctcaatact tctattgtta tgcctccaaa
                                                                  660
                                                                  720
aaatctggta gagctctttg gcaaactggc gagtggcaga tatctgcctc aaacttatgt ...
                                                                  780
ggttcgagaa gacctagttg ctgtggagga aattcgtgat gttagtaacc ttggcatctt
                                                                  840
tatttaccaa ctttgcaata acagaaagtc cttccgcctt cgtcgcagag acctcttgct
gggtttcaac aaacgtgcca ttgataaatg ctggaagatt agacacttcc ccaacgaatt
                                                                  900
tattgttgag accaagatct gtcaagagta agaggcaaca gatagagtgt ccttggtaat
                                                                  960
aagaagtcag agatttacaa tatgacttta acattaaggt ttatgggata ctcaagatat
                                                                 1020
                                                                 1080
1082
aa
<210> 516
<211> 559
<212> DNA
<213> Homo sapiens
<400> 516
etgetecage getgaegeeg agecatggeg gaegaggage ttgaggeget gaggagaeag
                                                                   60
aggetggeeg agetgeagge caaacaeggg gateetggtg atgeggeeca acaggaagca
                                                                  120
aagcacaggg aagcagaaat gagaaacagt atcttagccc aagttctgga tcagtcggcc
                                                                  180
                                                                   240
cgggccaggt taagtaactt agcacttgta aagcctgaaa aaactaaagc agtagagaat
taccttatac agatggcaag atatggacaa ctaagtgaga aggtatcaga acaaggttta
                                                                   300
atagaaatcc ttaaaaaagt aagccaacaa acagaaaaga caacaacagt gaaattcaac
                                                                   360
agaagaaaag taatggactc tgatgaagat gacgattatt gaactacaag tgctcacaga
                                                                   420
ctagaactta acggaacaag tctaggacag aagttaagat ctgattattt actttgttta
                                                                   480
540
aaaaaaaaa aaaaaaaaa
                                                                   559
<210> 517
<211> 110
<212> PRT
<213> Homo sapiens
<400> 517
Met Phe Cys Pro Leu Lys Leu Ile Leu Leu Pro Val Leu Leu Asp Tyr
                                   10
Ser Leu Gly Leu Asn Asp Leu Asn Val Ser Pro Pro Glu Leu Thr Val
                               25
His Val Gly Asp Ser Ala Leu Met Gly Cys Val Phe Gln Ser Thr Glu
```

4.0

<210> 518 <211> 4544 <212> DNA <213> Homo sapiens

- 13

<400> 518

60 ccgagaaggg Cttcaggacg cgggaggcgc acttgcttca agtcgcgggc gtgggaacgg ggttgcaaaa cggggccttt ttatccgggc ttgcttccqg cgtcatggct caaaggqcct 120 tecegaatee ttatgetgat tataacaaat eeetggeega aggetaettt gatgetgeeg ggaggctgac tcctgagttc tcacaacgct tgaccaataa gattcgggag cttcttcagc 240 aaatggagag aggcctgaaa tcagcagacc ctcgggatgg caccggttac actggctggg 300 caggiatige tgigettiae tiacatetti atgatgiatt tggggaecet geetaectae 360 agttagcaca tggctatgta aagcaaagtc tgaactgctt aaccaagcgc tccatcacct 420 teetttgtgg ggatgeagge eecetggeag tggeegetgt getatateae aagatgaaea 480 atgagaagca ggcagaagat tgcatcacac ggctaattca cctaaataag attgatcctc 540 atgctccaaa tgaaatgctc tatgggcgaa taggctacat ctatgctctt ctttttgtca 600 ataagaactt tggagtggaa aagatteete aaageeatat teageagatt tgtgaaacaa 660 ttttaacctc tggagaaaac ctagctagga agagaaactt cacggcaaag tctccactga 720 tgtatgaatg gtaccaggaa tattatgtag gggctgctca tggcctggct ggaatttatt 780 actacctgat gcagcccagc cttcaagtga gccaagggaa gttacatagt ttggtcaagc 840 ccagtgtaga Ctacgtctgc cagctgaaat tcccttctqq caattaccct ccatqtataq 900 gtgataatcg agatctgctt gtccattggt gccatggcgc ccctggggta atctacatgc 960 tcatccaggc ctataaggta ttcagagagg aaaagtatct ctgtgatgcc tatcagtgtg 1020 ctgatgtgat ctggcaatat gggttgctga agaagggata tgggctgtgc cacggttctg 1080 cagggaatgc ctatgccttc ctgacactct acaacctcac acaggacatg aagtacctgt 1140 atagggcctg taagtttgct gaatggtgct tagagtatgg agaacatgga tgcagaacac 1200 cagacacccc tttctctctc tttgaaggaa tggctggaac aatatatttc ctggctgacc 1260 tgctagtccc cacaaaagcc aggttccctg catttgaact ctgaaaggat agcatgccac 1320 ctgcaactca Ctgcatgacc ctttctgtat attcaaaccc aagctaagtg cttccgttgc 1380 tttccaagga aacaaagagt caaactgtgg acttgatttt gttagctttt ttcagaattt 1440 atctttcatt cagttccctt ccattatcat ttacttttac ttagaagtat ccaaggaagt 1500 cttttaactt taatttccat ttcttcctaa agggagagtg agtgatatgt acagtgtttt gagattgtat acatatttc cagaacttgg aggaaatctt atttaagttt atgaatataa 1620 ccatctgtta ctgttctaaa aatgtttaaa agaaactcaa tacagataaa gataaatatg 1680 tgactattat tgggtattac acttcacttc tctttaatat ttttcctcca actggagggc 1740 agacaatttt ctgacttgct tttctctagg tggttcattt tgaaagggga cagaaatata 1800 actaaatgct tccaggagaa aaattccaag agttacaatc tggacttggt acctaaatat 1860 cattttttaa attcttgatg cctatttgga ctagaggtaa acatactttc agattggcct 1920 gtttttgtcg gtaaggcata cagccttcag aagccaacat ttttaatcaa aaacttataa 1980 aacatgatga tcattgtgaa aattctgagt tgaaggttag tttaagataa gctaacaata 2040 acagtotgtg ttttctctaa aataatotga gttttttgga actotttatt taaatatgtg 2100 tgtttttcag tattcaaata agatcaggaa gccaattttc tatgtatgaa tatgctttaa 2160 cctaggattt cagtccactc tgactgactt tctaaacttt aacttgggtt tttacagtga 2220 ctatgcatta gtgctgactc tttggtataa gccataaaat attttccttc ctatcaattt 2280 atctgaactt tggtcttttc actaaattgt acagtattct acttctgttt aaaaagggga 2340 gatgagaaag ggaatactat ctaaccaata acttgaacaa aaacactaaa ctaagcattt 2400 aatagaaatg Ctttttattg aggaggtatt atccagagtt catgcttaga acaaatgcat 2460 ctttgcgtat cctagactta acaattcatc agtttctgag accacagaat caggttttcc 2520 gtagtagata aagactetet ggtgetteaa attetgttea agtgttttga eteateaget 2580 tetactettt etattaetge etttgeetgg ettgtttigt etetttgeaa etgattttge 2640 aaaaaaaaat tgtagcttta aaataacagg gtctaagtat tttaaatgtg cctatttcac 2700

agctctcttg	gtčacaaaaa	catgctattt	ttattggaac	ttcaaaccaa	atccccactg	2760
agtgtgtact	ggttcctgca	ggtagcagtc	tcctattatc	tcctgtttag	caccaaaaga	2820
gctaatatta	ttggaaactg	accttttaaa	ggccactggc	agtaggattt	aaaaagcagc	2880
ccactgctca	gtttccagga	tcagcttcct	ccttctgtca	cttgtgtaag	ttggcactac	2940
cttgtgcctc	tcagattgct	gaagtgctgc	tggtaagcat	gtgcatgctc	tgcctttctt	3000
gtgaaagttt	tcaatcagcg	atatcagcac	ttacagtaag	aagtaaaagt	agtgcacagc	3060
aaagctaatt	tgcctttgcc	tggggtgttc	agcttgaaag	aataaagctc	atttggttta	3120
gttaaatgtc	ttactctact	gtgcctatgc	ttttagctgc	gttactaagc	aagggaaaaa	3180
taacagtttc	tctgagccag	agaagacttg	atcacagttc	tccaagcatc	gtgatagcaa	3240
tgcttaaccc	caggaagatt	tcaaggcagg	gagaagaaca	tttcaaataa	gattcttgtt	3300
aacccattta	tgcctagtgt	tccattattg.	gaatgctaag	cttgtgggag	tcatttacat	3360
cctactgctc	aaagtcattg	ccaaggtctg	atttttcaca	caaaaaattg	caacccccag	3420
cataaatggg	ttagctactg	tcatcagtta	.gcaaattcat	ccacacaaac	acaattagag	3480
tttggttttt	ttttaagctt	ttcaaaactt,	actaaactgg	cacaatttta	tatgtatgct,	3540
atttgttgta	tttatgctta	agagcaaaaa	agttttgatg	ggattttaaa	ttcagcaaag	3600
cctacaacgc	tgágacaatc	ccctaacaac	atggtagtaa	ctaaagaaac	ttttatacta	3660
ggcttcttag	ttttaaaagg	aagtggcatc	attgtttcag	ttctagtttg	tatttttctc	3720
tcagatattt	ttcttcttta	aaaatctttc	ccagaagttg	gttcctagaa	aactcaatac	.3780
catcatctct	tatctctata	cagggactag	gtaataaaac	cttcaaaggt	tgtcaaaggt	3840
			tgtttctgtt			3900
gcaaatagtt	aacttttcat	catgtaaaaa	gttaacatta	tcctatttcc	atagatacca	3960
tggacggcgg	tgtggcctga	gttgtcagtc	tttaatcctg	agtcatgtgg	ctctctttc	4020
atctttgatg	tcagttccaa	ttatttggca	tcaaaaacct	tcatggtagg	tagagtttta	4080
ggtaaaagtg	gatctagggt	tactttcttt	attaacattt	cctaaataac	tgaattgaga	4140
gacatactct	gctactatgt	cctcaggtta	atttttgtct	gatcttacga	tgccctgcct	4200
tttactagct	actttagaaa	tagaaaatgt	gaagagtgac	tatttacatg	tatactcctt	4260
tggctgctag	aactcatctg	tagtccttta	ttatttacac	tgaattccaa	tttcatttct	4320
cttccgctaa	gtaagagcac	ctcattcctg	tgttttctct	actattgagc	tgtagacgaa	4380
ctgtttctct	aattataaag	caaactgttt	gggatattca	gggaaactac	cccaatgtta	4440
tgttgtcatt	taatgggaaa	ggctgggatc	atatgtattt	ctatgttctg	taaagtattt	4500
gacttactag	ttctcaataa	aattttatta	ggactataaa	aaaa		4544

<210> 519 <211> 1779

<212> DNA

<213> Mus musculus

#### <400> 519

ggtccggaat tcccgggtcg acccacgcgt ccgctggcct tgggcgcaga ccccggccgg 60 tecegggget geetetttaa gggagggggt ggageegega gteaggegeg aggageteea 120 gaaatettga ggecagagee eegeaeeteg gegeageeat gagtgeggag gtgaaggtga 180 cagggcagaa ccaagagcag tttctgctcc ttgccaagtc ggctaagggg gcggcactgg 240 ccacactcat ccaccaggtg ctggaggccc ctggtgtcta cgtgtttggg gaactgctgg 300 atatgeetaa tgttagagag etggeagaaa gegaetttge etceaeette eggetgetea 360 cagtgtttgc ctatgggacc tatgcggact acttagctga agccaggaat ctcccccac 420 tgactgacgc acagaagaat aagcttcgac atctgtcagt tgtcactctg gctgccaaag 480 tcaagtgtat cccatatgca gtgttgctgg aggcccttgc ccttcgaaac gtgcgccagc 540 tggaagacct tgtgatcgag gctgtgtatg ctgatgtcct tcgtggctct ctggaccagc 600 gcaatcagcg gctagaggtt gattacagca tcgggcggga catccagcgc caggacctca 660 gtgccatcgc ccagaccctg caagagtggt gcgtgggctg tgaggttgtg ttgtcgggca 720 tcgaagagca ggtcagccgt gccaaccagc acaaggagca gcagctgggc ctgaagcagc 780 agatcgaaag tgaggttgcc aaccttaaga aaaccattaa agttacgaca gcagctgctg 840 ctgcagccac ctcccaggat cctgagcaac acctgacaga gctgagagaa ccagcttctg 900 gcaccaacca gcgccagccc agcaagaaag cctccaaggg caagggactc cgagggagcg 960 ccaagatttg gtccaagtcg aactgaaagg acttgtttct tccctgggaa tgtggggtcc 1020 cagctgccta cctgcctacc ccttaggagt cctcagagcc ttcctgtgcc cctggccagc 1080 tgataatgct agttcattac ttttcatctc ctccaccccc aagcataagc cacaccctct 1140 gtagggagga ggccagtgca ggtcatgttc tgttggtacc tcttatgtgt tccatgctct 1200 tecceageae gettgetete ategttttte egeaetgtgt etgeceatta eccetgteat 1260 tgagcaggtt ggcagtccta tggagggtgc tggctcttaa ccacccacac ctacccctgc 1320

atqcctaatc	tgcagttcct	cctcctcccc	ttgcctagtg	ggctgcatct	gaaaagccat	1380
ggggaagggg	gtctccacct	tcattccagc	cttagagttc	tggagccagt	ctgctaccct	1440
gggagtcgct	ggacattttc	ctcccaqaac	cccatcacac	tacaattgtt	tctttcctct	1500
ctcatctcct	tgggcctggg	gatactgctg	cttcagtgac	cccagageet	gagaacagct	1560
attttgaga	tgttaagaaa	taattettta	ttactcatca	tcttaggaag	cccaatggaa	1620
atectegase	gatttatatc	tectectata	attctaataa	qqaaqqaaat	atagattgta	1680
					acacagaaat	1740
	gaaatgtatg				J	1779
aaatytatya	gaaatgtatg	Lacadadad	daaaaaaaa			-

## **PCT**

# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : C12N 15/12, C07K 14/47, 16/18, C12Q		(11) International Publication Number: WO 99/3123		
1/68	Ĺ.,	(43) International Publication Date:	24 June 1999 (24.06.99)	
(21) International Application Number: PCT/IB9 (22) International Filing Date: 17 December 1998 (		BY, CA, CH, CN, CU, CZ, DE,	, DK, EE, ES, FI, GB, GE	
9 9		KZ, LC, LK, LR, LS, LT, LU,		
(30) Priority Data: 60/069,957 60/074,121 9 February 1998 (09.02.98) 60/081,563 13 April 1998 (13.04.98) 60/096,116 10 August 1998 (10.08.98)	΄ τ τ	MW, MX, NO, NZ, PL, PT, RC SL, TJ, TM, TR, TT, UA, UG ARIPO patent (GH, GM, KE, L Eurasian patent (AM, AZ, BY, K European patent (AT, BE, CH, GB, GR, IE, IT, LU, MC, NL, BJ, CF, CG, CI, CM, GA, GN TD, TG).	B, US, UZ, VN, YU, ZW, S, MW, SD, SZ, UG, ZW, KG, KZ, MD, RU, TJ, TM), CY, DE, DK, ES, FI, FR, PT, SE), OAPI patent (BF,	
(71) Applicant (for all designated States except US): [FR/FR]; 24, rue Royale, F-75008 Paris (FR).	GENSI	T	·	
[110116], 24, 140 Noyale, 1-75000 14115 (116).		Published		
(72) Inventors; and		With international search report.		
(75) Inventors/Applicants (for US only): BOUGUELER die [FR/FR]; 108, avenue Victor Hugo, F-92170 (FR). DUCLERT, Aymeric [FR/FR]; 6 ter, rue VF-94100 Saint-Maur (FR). DUMAS MILNE ED Jean-Baptiste [FR/FR]; 8, rue Grégoire de Tours, Paris (FR).	Vanv Victorii WARD	and to be republished in the event of e, (88) Date of publication of the internation	the receipt of amendments	
(74) Agents: MARTIN, Jean-Jacques et al.; Cabinet Re 26, avenue Kléber, F-75116 Paris (FR).	gimbea	u,		
$_{0}$ $\alpha$				

#### (54) Title: EXTENDED cDNAs FOR SECRETED PROTEINS

### (57) Abstract

The sequences of extended cDNAs encoding secreted proteins are disclosed. The extended cDNAs can be used to express secreted proteins or portions thereof or to obtain antibodies capable of specifically binding to the secreted proteins. The extended cDNAs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. The extended cDNAs may also be used to design expression vectors and secretion vectors.

# FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
ΑT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
ΑZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TĐ	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
ВG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
ВJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

International Application No // IB 98/02122

a. CLASSIFICATION OF SUBJECT MATTER IPC 6 C12N15/12 C07 C07K14/47 C07K16/18 C12Q1/68 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) C12N C07K C12Q IPC 6 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No E.L WO 99 06549 A (GENSET (FR); DUMAS MILNE 1-20 EDWARDS J.-B.; DUCLERT A.; LACROIX B.) 11 February 1999 (1999-02-11) L: Priority abstract page 6 - page 12 page 129 - page 133; claims Seq. ID: 251 page 213 - page 214 Seq. ID: 484 page 366 - page 367 X 2,5,8 Database EMBL, entry HS695112 Accession number R50695 24 May 1995 95% identity with Seq.ID:40 nt.1-384 XP002097725 the whole document -/--Further documents are listed in the continuation of box C. Х Patent family members are listed in annex. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but "A" document defining the general state of the art which is not cited to understand the principle or theory underlying the considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to "L" document which may throw doubts on priority claim(s) or involve an inventive step when the document is taken alone which is cited to establish the publication date of another "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such docu-\*O\* document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. other means document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report **2** 7. 07. 99 24 March 1999 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Macchia, G Fax: (+31-70) 340-3016

International Application No F / IB 98/02122

	Ition) DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Melevant to claim No.
A	WO 96 34981 A (GENSET (FR); NICOLAEVNA MERENKOVA I.; DUMAS MILNE EDWARDS JB.G.) 7 November 1996 (1996-11-07) cited in the application abstract	· .
<b>A</b>	EP 0 625 572 A (KANAGAWA ACAD OF SCIENCE AND TECHNOL FOUNDATION (JP); KATO S; SEKINE S) 23 November 1994 (1994-11-23) cited in the application abstract	
A	CARNINCI P. ET AL.: "High-efficiency full-length cDNA cloning by biotinylated CAP trapper" GENOMICS, vol. 37, no. 3, 1 November 1996 (1996-11-01), pages 327-336, XP002081729 cited in the application abstract	
A	KATO S. ET AL.: "Construction of a human full-length cDNA bank" GENE, vol. 150, 1994, pages 243-250, XP002081364 cited in the application abstract	÷
A	WO 97 07198 A (GENETICS INSTITUTE INC (US); JACOBS K; MCCOY JM; KELLEHER K; CARLIN M) 27 February 1997 (1997-02-27)	
A	TASHIRO K. ET AL.: "Signal sequence trap: a cloning strategy for secreted proteins and type I membrane proteins" SCIENCE, vol. 261, 30 July 1993 (1993-07-30), pages 600-603, XP000673204 abstract	
A	YOKOYAMA-KOBAYASHI M. ET AL.: "A signal sequence detection system using secreted protease activity as an indicator" GENE, vol. 163, 1995, pages 193-196, XP002053953 abstract	
A	HEIJNE VON G.: "A new method for predicting signal sequence cleavage sites" NUCLEIC ACIDS RESEARCH, vol. 14, no. 11, 1986, pages 4683-4690, XP002053954 cited in the application abstract	

International Application No
7/IB 98/02122

C.(Continua	tion) DOCUMENTS CONSIDERED TO BE RELEVANT	7/1B 98/02122
Category <sup>a</sup>	Citation of document, with Indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LOCKHART D.J. ET AL.: "Expression monitoring by hybridization to high-density oligonucleotide arrays" BIO/TECHNOLOGY, no. 14, 14 December 1996 (1996-12-14), pages 1675-1680, XP002074420 abstract	18
	<del></del>	
٠.		
		·
	·	
•		

International application No.

PCT/IB 98/02122

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.:     because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
See additional sheet.
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  Invention 1, Claims 1-20 partially.
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: Invention 1: Claims 1-20, all partially.

Nucleic acid comprising the sequence as in Seq.ID:40, complementary sequence or fragments, host cell containing said nucleic acid. Polypeptide as in Seq.ID:141, encoded by said polynucleotide, or fragments, method of making said polypeptide. Antibody specifically binding to said polypeptide.

2. Claims: Inventions 2-233: Claims 1-20, all partially, as far as applicable.

Idem as subject 1 but limited to each of the DNA sequences as in Seq.ID:41-140, 242-377, and corresponding polypeptides, where invention 2 is limited to Seq.ID:41 and 142, invention 3 is limited to Seq.ID:42 and 143, ...., invention 8 is limited to Seq.ID:47 and 148, invention 9 is limited to Seq.ID:48,49,110,149,150 and 211, invention 10 is limited to Seq.ID:50 and 151, ...., invention 32 is limited to Seq.ID:72 and 173, invention 33 is limited to Seq.ID:73,74,131,174,175 and 232, invention 34 is limited to Seq.ID:75 and 176, ...., invention 233 is limited to Seq.ID:377 and 513.

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

Information on pater.t family members

International Application No
F /IB 98/02122

Patent document cited in search report			Publication date		tent family tember(s)	Publication date	
WO	9906549	Α	11-02-1999	AU	8555098 A	22-02-1999	
WO	9634981	A	07-11-1996	FR FR AU CA EP	2733765 A 2733762 A 5982996 A 2220045 A 0824598 A	08-11-1996 08-11-1996 21-11-1996 07-11-1996 25-02-1996	
EP	0625572	Α	23-11-1994	JP WO US	6153953 A 9408001 A 5597713 A	03-06-1994 14-04-1994 28-01-1997	
wo	9707198	A	27-02-1997	US AU AU CA CA EP EP WO	5707829 A 6712396 A 6768596 A 2227220 A 2229208 A 0839196 A 0851875 A 9704097 A	13-01-1998 18-02-1997 12-03-1997 06-02-1997 27-02-1997 06-05-1998 08-07-1998 06-02-1997	